J Pediatr (Rio J). 2020;96(5):630–637

Jornal de Pediatria
www.jped.com.br

ORIGINAL ARTICLE

# Association between the *FTO* gene polymorphism and obesity in Brazilian adolescents from the Northeast region☆,☆☆

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Received 24 February 2019; accepted 13 May 2019
Available online 30 July 2019

**KEYWORDS**
Cohort;
Body fat;
rs9939609
Polymorphism

**Abstract**
*Objective:* To investigate the association between the *FTO* gene polymorphism with obesity in Brazilian adolescents from the Northeast region.
*Method:* This was a case–control study with adolescents aged 18 to 19 years. The case group consisted of 378 obese individuals and the control group of 378 non-obese individuals. Obesity was measured by percentage of body fat using the air displacement plethysmography technique. The study variables included data on socioeconomics, demographics, lifestyle, physical activity, waist circumference, waist-to-height ratio, and body mass index. To identify the rs9939609 polymorphism of the *FTO* gene, blood samples were obtained for genomic DNA extraction by the real-time PCR (Polymerase Chain Reaction) technique. Categorical variables were compared between the groups by the chi-squared test. The normality of the anthropometric measurements body mass index, waist circumference, waist-to-height ratio, and percentage of body fat was evaluated by the Shapiro–Wilk test. Comparison of the anthropometric measurements, stratified by the polymorphism genotypes, was performed by the Kruskal–Wallis test. The Hardy–Weinberg equilibrium was calculated. The significance level was set at 5%.
*Results:* The variables gender, age, and physical activity showed significant differences between the groups ($p < 0.001$). The samples of obese and non-obese adolescents were in Hardy–Weinberg equilibrium ($p = 0.0515$). There was no significant difference between the genotypic ($p = 0.719$) and allelic frequencies ($p = 0.812$) regarding the case and control groups. When comparing the anthropometric measurements according to the genotypes (AA, AT, and TT), no significant difference was observed for body mass index ($p = 0.337$), waist circumference ($p = 0.3473$), percentage of body fat ($p = 0.7096$), and waist-to-height ratio ($p = 0.2584$).

☆ Please cite this article as: Rodrigues LS, Santos AM, Lima MI, Simões VM, Pereira SR. Association between the *FTO* gene polymorphism and obesity in Brazilian adolescents from the Northeast region. J Pediatr (Rio J). 2020;96:630–7.
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https://doi.org/10.1016/j.jped.2019.05.006

*Conclusion:* The excess adiposity of the study adolescents was not influenced by their genotype.


**PALAVRAS-CHAVE**
Coorte;
Gordura corporal;
Polimorfismo rs9939609

## Relação do polimorfismo do gene FTO com a obesidade em adolescentes do nordeste brasileiro

### Resumo

*Objetivo:* Investigar a relação do polimorfismo do gene *FTO* com obesidade em adolescentes no Nordeste brasileiro.

*Método:* Estudo caso-controle realizado com adolescentes de 18 a 19 anos. O grupo caso foi formado por 378 indivíduos obesos e o controle por 378 não obesos. Obesidade foi medida pelo percentual de gordura corporal pela técnica de pletismografia por deslocamento de ar. Variáveis em estudo englobam dados socioeconômicos, demográficos, hábitos de vida, atividade física, circunferência da cintura, razão cintura-estatura e índice de massa corporal. Para identificação do polimorfismo rs9939609 do gene *FTO* foram obtidas amostras de sangue para extração do DNA genômico pela técnica de PCR em tempo real. Variáveis categóricas foram comparadas entre os grupos pelo teste qui-quadrado. Normalidade das medidas antropométricas índice de massa corporal, circunferência da cintura, razão cintura-estatura e percentual de gordura corporal foram avaliados pelo teste Shapiro-Wilk. Comparação das medidas antropométricas, estratificadas pelos genótipos do polimorfismo, foi realizada pelo teste Kruskall-Wallis. Calculou-se o equilíbrio de Hardy-Weinberg. Nível de significância adotado de 5%.

*Resultados:* As variáveis sexo, idade e atividade física apresentaram diferenças significativas entre os grupos ($p < 0{,}001$). As amostras dos adolescentes obesos e não obesos estavam em equilíbrio de Hardy-Weinberg ($p = 0{,}0515$). Não houve diferença significante entre as frequências genotípicas ($p = 0{,}719$) e alélicas ($p = 0{,}812$) em relação aos grupos caso e controle. Quando comparadas as medidas antropométricas segundo os genótipos (AA, AT e TT), não foi observada diferença significante do índice de massa corporal ($p = 0{,}3337$), circunferência da cintura ($p = 0{,}3473$), percentual de gordura corporal ($p = 0{,}7096$) e razão cintura-estatura ($p = 0{,}2584$).

*Conclusão:* O excesso de adiposidade dos adolescentes em estudo não foi influenciado pelo genótipo.



## Introduction

Obesity, characterized by an excessive accumulation of body fat, brings complications that can be often observed in increasingly younger individuals. Some factors are related to this picture, among them environmental factors, the individual's lifestyle, differentiated diet, and environmental contaminants that can act as endocrine disruptors.[1]

The adolescents' social conditions are defined according to the environment where they live.[2] In this sense, the diet at this stage is highly caloric, with ingestion of ultra-processed products, in addition to inadequate life habits, such as sedentary lifestyle and excessive use of electronic equipment, which are aspects that contribute to the development of obesity.[3] Additionally, the genetic makeup of the individual may also contribute to the onset of obesity, especially when associated with an inadequate lifestyle.[4]

Obesity contributes to the onset of non-communicable chronic diseases (NCCDs).[2] According to Afmanand Müller,[5] the NCCDs, such as type 2 diabetes mellitus (T2DM), metabolic syndrome (MS), and cardiovascular diseases (CVDs),result from these associations of environmental and genetic factors, interfering in people's lives when they are obese or overweight.

Approximately 70% of obese children and adolescents tend to become obese adults as well.[6] Excess weight is associated with a gradual increase in the risk of morbidity and mortality in adulthood, since obesity is one of the risk factors for noncommunicable diseases and disorders, being the main causes of death in adults.

This can lead to an increased risk of premature death and disability in adult life, as in Brazil, among adolescents (10–19 years), at least one-fifth had excess weight and 4.9% were obese, with higher indices in the male population and in the age group of 10–11 years old.[7]

From the genetic point of view, different polymorphisms have been described in the literature as being associated with obesity.[8] Among these, the fat mass and obesity-associated gene (*FTO*) has single-nucleotide polymorphisms (SNPs) associated with the metabolism alteration process and, therefore, their presence has a direct association with the status of obesity, overweight, and other pathologies.[9]

The most often investigated *FTO* gene polymorphism that is associated with obesity is rs9939609, characterized by the

substitution of T by A in intron 1. Studies indicate that individuals who are homozygous for the risk allele (A allele) are approximately 3 kg heavier or more, and have a 1.7-fold increased risk of being obese when compared to those with homozygotes for the T allele.[10] Hunt et al.[11] demonstrated that this SNP is associated with an increased risk of adult individuals developing obesity and other NCCDs.

In Brazil, Silva et al.[12] carried out a study with children and adolescents from Rio Grande do Sul, with a sample of 348 children followed from birth to 8 years of age, and another one consisting of 615 children and adolescents from 4 to 18 years of age. The authors observed that individuals with the A/A genotype had a higher Z-score for body mass index (BMI), abdominal circumference, and skinfolds. However, Souza et al.[13] carried out a study with adults and children, also in Brazil, and observed the absence of association between the *FTO* gene and the anthropometric measures used in the comparisons.

It is evident that, for the most part, the studies that associate *FTO* gene polymorphisms and obesity were carried out with adult populations and in European and or Asian countries or in Brazilian regions predominantly of European descent, where populations are genetically more homogeneous when compared those of the Latin American countries, which are typically mixed-race.[14] Therefore, very often the results are not necessarily the same in different ethnic groups or groups organized by age range.

Thus, the aim of this study was to investigate the association of a polymorphism in the *FTO* gene with obesity in adolescents from the municipality of São Luís, Maranhão, Brazil.

## Methods

### Study type

This was a case-control study with adolescents (18 to 19 years) from the RPS Cohort of São Luís, Maranhão. The RPS cohort encompasses the cities of Ribeirão Preto, state of São Paulo; Pelotas, state of Rio Grande do Sul; and São Luís, state of Maranhão, whose main objective was to evaluate the health of individuals born in 1997 and to monitor their health until adulthood. For that purpose, data were collected periodically on breastfeeding, home stimulation, mental disorders, violence, nutrition, body composition, sleep, physical activity, and genetic factors, among others.

### Study population and sample

The study population consisted of 2515 adolescents. Adolescents without information on the main variables (percentage of fat, weight, height, gender, and age) were excluded from the study. Therefore, the population consisted of 2382 adolescents.

The sample size was calculated considering a 95% confidence level, and a power of 80%; the odds ratio (OR) was estimated a priori at 2.0, with a frequency of 16%[10] for the rs9939609 SNP of the *FTO* gene in individuals homozygous for the risk allele (A) and with a ratio of one case to one control. Thus, 682 adolescents were necessary, *i.e.*, 341 cases and 341 controls.

Adolescents with a percentage of body fat (%BF) > 25% (boys) and >30% (girls) were defined as obese (cases), totaling 629 adolescents. The controls comprised girls with %BF $\leq$ 30% and boys with %BF $\leq$ 25% ($n$ = 1753). In both groups, the adolescents were randomly selected considering the minimum sample size of each group, and all adolescents included were eligible.

The study included 782 adolescents, but there was no amplification in the sample of 26 adolescents, who were excluded from the study. Thus, the final sample consisted of 756 adolescents, 378 in the non-obese group (control) and 378 of the obese group (case).

### Socioeconomic and demographic data, life habits

The assessed socioeconomic and demographic variables were as follows: age, gender, family income, level of schooling, ethnicity/skin color, number of people living in the household, and the Brazilian Economic Classification Criteria, marital status, separated or divorced parents, occupation, and smoking status. This information was obtained through a structured interview, according to the standardized questionnaires of the RPS Cohort.

The Mini International Neuropsychiatric Interview (M.I.N.I.) – Brazilian version 5.0.0 – DSM IVis an interview focused on the diagnosis of mental disorders such as the antisocial personality and risk of suicide; however, only information related to alcohol consumption was used.[15] When asked about how frequently they consumed drinks containing alcohol, the present study considered as ''no'' for those who answered ''never'' and ''yes'' for those who said they consumed alcohol ''once or more than once a week.''

The physical activity level was evaluated through the 24-h Physical Activity Recall, created from the Self-Administered Physical Activity Checklist (SAPAC),[16] classified as sedentary, low, moderate, or high.[17]

### Anthropometric and nutritional assessment

Weight measurements (in kg) were performed using a Filizola® (Filizola, SP, Brazil) scale coupled to an air displacement plethysmography (ADP) system. The participants were asked to stand barefoot, standing upright in the center of the scale, wearing the least possible clothing, head oriented in the horizontal Frankfurt plane and wearing no accessories, to undergo the measurement of height in centimeters, with the aid of an Alturexata® (Alturexata, MG, Brazil) portable stadiometer. Based on these data, the BMI was calculated by the ratio: body weight (kg)/height ($m^2$). Measurements of waist circumference (WC) were obtained, consisting of the measurement (in cm) at the midpoint between the iliac crest and the last rib. Each participant was measured twice, and the final result was the average of the two measurements.

The participants' proportion of central fat by height was evaluated through the waist-to-height ratio (WHtR), calculated by dividing the waist circumference (cm) by height (cm). The points were determined according to Ashwell and Hsieh,[18] indicated for adolescents of both genders, considering values below 0.50 to be adequate.

**Table 1** Socioeconomic, demographic, and lifestyle characteristics of participants from the Ribeirão Preto, Pelotas, and São Luís, (RPS) Cohort of São Luís, Maranhão, Brazil, 2019.

| Variables | Total | | Non-obese | | Obese | | *p*-Value |
|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *n* | % | |
| *Gender* | | | | | | | |
| Male | 295 | 39.02 | 223 | 58.99 | 72 | 19.05 | <0.001 |
| Female | 461 | 60.98 | 155 | 41.01 | 306 | 80.95 | |
| *Age (years)* | | | | | | | |
| 18 | 500 | 66.14 | 267 | 70.63 | 233 | 61.64 | 0.009 |
| 19 | 256 | 33.86 | 111 | 29.37 | 145 | 38.36 | |
| *Ethnicity* | | | | | | | |
| White | 166 | 22.05 | 78 | 20.63 | 88 | 23.47 | 0.585 |
| Black | 121 | 16.07 | 64 | 16.93 | 57 | 15.20 | |
| Mixed-race | 466 | 61.89 | 236 | 62.43 | 230 | 61.33 | |
| *Marital status* | | | | | | | |
| Single | 725 | 95.90 | 363 | 96.03 | 362 | 95.77 | 0.640 |
| Married | 8 | 1.06 | 5 | 1.32 | 3 | 0.79 | |
| Common-law marriage | 23 | 3.04 | 10 | 2.65 | 13 | 3.44 | |
| *Level of schooling* | | | | | | | |
| A/ FI-i | 1 | 0.13 | 0 | 0.00 | 1 | 0.26 | |
| FI-c/ FII-i | 1 | 0.13 | 1 | 0.26 | 0 | 0.00 | 0.120 |
| FII-c/ M-i | 239 | 31.61 | 132 | 34.92 | 107 | 28.31 | |
| M-c/ S-i | 515 | 68.12 | 245 | 64.81 | 270 | 71.43 | |
| *Employed* | | | | | | | |
| No | 646 | 85.45 | 323 | 85.45 | 323 | 85.45 | 1.000 |
| Yes | 110 | 14.55 | 55 | 14.55 | 55 | 14.55 | |
| *Family income (minimum wages)* | | | | | | | |
| <1 | 129 | 17.06 | 72 | 19.05 | 57 | 15.08 | |
| 1 < 2 | 213 | 28.17 | 113 | 29.89 | 100 | 26.46 | 0.118 |
| 2 < 3 | 118 | 15.61 | 57 | 15.08 | 61 | 16.14 | |
| 3 < 4 | 75 | 9.92 | 37 | 9.79 | 38 | 10.05 | |
| ≥4 | 118 | 15.61 | 60 | 15.87 | 58 | 15.34 | |
| Unknown | 103 | 13.62 | 39 | 10.32 | 64 | 16.93 | |
| *Separated/divorced parents* | | | | | | | 0.610 |
| No | 393 | 51.98 | 193 | 51.06 | 200 | 52.91 | |
| Yes | 363 | 48.02 | 185 | 48.94 | 178 | 47.09 | |
| *CCEB* | | | | | | | |
| Class A | 63 | 8.34 | 27 | 7.16 | 36 | 9.52 | |
| Class B | 491 | 65.03 | 242 | 64.19 | 249 | 65.87 | 0.237 |
| Class C | 199 | 26.36 | 106 | 28.12 | 93 | 24.60 | |
| Classes D–E | 2 | 0.26 | 2 | 0.53 | 0 | 0.00 | |
| *Physical activity level* | | | | | | | |
| Sedentary | 373 | 49.47 | 145 | 38.56 | 228 | 60.32 | |
| Low | 93 | 12.33 | 49 | 13.03 | 44 | 11.64 | <0.001 |
| Moderate | 167 | 22.15 | 101 | 26.86 | 66 | 17.46 | |
| High | 121 | 16.05 | 81 | 21.54 | 40 | 10.58 | |
| *Smoker* | | | | | | | |
| No | 728 | 96.55 | 365 | 97.07 | 363 | 96.03 | 0.433 |
| Yes | 26 | 3.45 | 11 | 2.93 | 15 | 3.97 | |
| *Alcohol consumption* | | | | | | | |
| No | 437 | 58.03 | 216 | 57.60 | 221 | 58.47 | 0.810 |

Table 1 (*Continued*)

| Variables | Total | | Non-obese | | Obese | | *p*-Value |
|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *n* | % | |
| Yes | 316 | 41.97 | 159 | 42.40 | 157 | 41.53 | |

A, illiterate; FI-I, incomplete elementary school; FI-c, complete elementary school; FII-I, incomplete junior high; FII-c, complete junior high; M-I, incomplete high school; M-c, complete high school; S-I, incomplete college/university; CCEB, Brazilian Economic Classification Criteria. *p*-value, significant when < 0.05.

The nutritional status of the adolescents was evaluated by the BMI, adopting as the classification criteria the values for age and gender and the respective cutoff points proposed by the World Health Organization[19] for individuals aged 10.0–19.0 years; for young individuals older than 19.0 years, the World Health Organization classification was followed.[20]

The evaluation of total body fat was performed using the ADP method in the COSMED Bod Pod® (Teprel, Porto, Portugal) gold standard device. The %BF was estimated using Siri's equation.[21] According to the classification by Williams et al.,[22] boys with a %BF > 25% and girls > 30% were considered as having excess weight.

## FTO gene polymorphism

Samples of 5 mL of whole blood were collected from the cubital vein and stored under refrigeration. Genomic DNA was extracted using the DNA Blood Mini Kit (Qiagen, CA, United States) using a QIA cube automated extractor (Qiagen, CA, United States), according to the manufacturer's recommendations. Then, they were stored in a freezer at −20 °C for an indeterminate period in order to avoid possible loss of material or contamination.

A NanoDrop spectrophotometer (Termo Scientific, CA, United States), was used for the quantification of the extracted DNA, according to the manufacturer's instructions.

The analysis of the rs9939609 SNP of the *FTO* gene was performed using the rhAmp™ SNP Genotyping System (Integrated DNA Technologies, IA, United States) assay on a 7500 Fast System real-time PCR system (Applied Biosystems, CA, United States). The reagents were purchased commercially and used according to the manufacturer's standards.

## Statistical analysis

The statistical analysis was performed using the statistical software STATA (Stata Statistical Software: Release 14. College Station, TX, United States). The normality of the anthropometric measures (BMI, WC, WHtR, and %BF) was evaluated by the Shapiro–Wilk test. The study variables in the case group were compared with those in the control group, using the chi-squared test.

The Hardy–Weinberg equilibrium was calculated for the genetic data.[23] The Kruskal–Wallis test was used to compare the means of anthropometric measures stratified by the different genotypes of the rS9939609 polymorphism of the *FTO* gene. In all tests, the significance level was set at 5%.

## Ethical considerations

The study was approved by the Research Ethics Committee of Hospital Universitário da Universidade Federal do Maranhão (No. 1,302,489), in accordance with national health council Resolution No. 466/2012 and CNS Operational Rule No. 001 of 2013.

## Results

The total sample consisted of 461 girls and 297 boys, with a mean age of 18.34 years. The case group was characterized by 80.95% female subjects; 61.64% were aged 18 years or younger; 61.33% were mixed-race; 95.77% were single; 71.43% were in high school or college/university; 85.45% did not work; 26.46% had a family income of one to two minimum wages; 52.91% had non-separated parents; 65.87% were classified as belonging to social class B. Regarding lifestyle, 60.32% were sedentary, 96.03% were non-smokers, and 58.47%% did not consume alcoholic beverages (Table 1).

In the control group, 58.99% of the individuals were males; 70.63% were aged 18 years; 62.43% declared themselves as mixed-race; 96.03% were single; 64.81% of adolescents had finished high school or were attending college/university; 85.45% did not work; 29.89% had a family income of one to two minimum wages in the month prior to the interview; 51.06% had separated parents, and 64.19% were in social class B. Regarding lifestyle, 49.47% were sedentary, 97.07% were nonsmokers, and 57.60% did not drink alcohol. Only the variables gender, age, and physical activity showed statistically significant differences between the groups ($p < 0.001$; Table 1).

The case and the control groups were in Hardy–Weinberg equilibrium ($p = 0.0515$). The distribution of the rs9939609 polymorphism was not statistically different in relation to the genotypic ($p = 0.719$) and allelic frequencies ($p = 0.812$; Table 2).

Regarding the anthropometric measures of the total sample according to the adolescents' genotype, there was no statistically significant difference between the means of BMI ($p = 0.337$), WC ($p = 0.343$), %BF ($p = 0.7096$), and WHtR ($p = 0.2584$) when comparing the different genotypes (Table 3).

For comparison purposes, results from studies evaluating the association between obesity and the rs9939609 polymorphism of *FTO* gene are shown. BMI or dual-energy

**Table 2** Genotypic and allelic frequencies of the rS9939609 polymorphism of the FTO gene in the Ribeirão Preto, Pelotas, and São Luís (RPS) Cohort of São Luís, Maranhão, Brazil, 2019.

| Gene (SNP) | Genotype | Non-obese (%BF) | | Obese (%BF) | | *p*-Value[a] |
|---|---|---|---|---|---|---|
| | | *N*: 378 | GF (%) | *N*: 378 | GF (%) | |
| *FTO* (rs9939609) | TT | 146 | 38.62 | 153 | 40.48 | 0.719 |
| | AT | 181 | 47.88 | 170 | 44.97 | |
| | AA | 51 | 13.49 | 55 | 14.55 | |
| | Alleles | N: 378 | AF (%) | N: 378 | AF (%) | |
| | T | 473 | 62.57 | 480 | 63.16 | 0.812 |
| | Ag | 283 | 37.43 | 280 | 36.84 | |

SNP, single-nucleotide polymorphism; %BF, percentage of body fat; GF, genotypic frequency; FTO, fat mass and obesity-associated gene; AF, allelic frequency, risk allele for obesity.
[a] Chi-squared test.

**Table 3** Comparison between the means of the anthropometric measures and genotype in the total sample of adolescents of the Ribeirão Preto, Pelotas, and São Luís (RPS) Cohort of São Luís, Maranhão, Brazil, 2019 ($n = 756$).

| Measure | *FTO*rs9939609 | | | | | | *p*-Value[a] |
|---|---|---|---|---|---|---|---|
| | A/A | | A/T | | T/T | | |
| | Mean | SD | Mean | SD | Mean | SD | |
| BMI | 23.56 | 4.26 | 23.03 | 4.24 | 23.47 | 4.40 | 0.3337 |
| WC | 84.16 | 7.98 | 83.75 | 9.27 | 84.92 | 9.87 | 0.3473 |
| %BF | 26.15 | 11.30 | 25.41 | 11.86 | 26.25 | 11.44 | 0.7096 |
| WHtR | 0.50 | 0.05 | 0.50 | 0.05 | 0.51 | 0.06 | 0.2584 |

FTO, fat mass and obesity-associated gene; SD, standard deviation; BMI, body mass index (kg/m$^2$); WC, waist circumference (cm); %BF, percentage of body fat; WHtR, waist-to-height ratio.
[a] Kruskal–Wallis test.

**Table 4** Prevalence of obesity and the allelic and genomic frequencies of different studies.

| Type of study | Obese individuals (%) | GF (%) | | | AF (%) | | References |
|---|---|---|---|---|---|---|---|
| | | TT | AT | AA | T | A | |
| Case–control | 53.3 | 20.0 | 23.1 | 22.6 | 46.9 | 49.5 | Pereira et al.[4] |
| Cross-sectional | 34.5 | 33.1 | 28.9 | 57.4 | 59.3 | 40.7 | Reuter et al.[23] |
| Cross-sectional | 12.0 | 77.0 | 22.0 | 1.0 | 87.0 | 13.0 | Flores et al.[24] |
| Cross-sectional | 35.1 | 74.4 | 23.4 | 2.1 | 86.2 | 13.8 | Xi et al.[25] |

GF, genotypic frequency; AF, allelic frequency.

X-ray absorptiometry (DXA) were used as the criterion to define obesity. Different prevalence rates of obesity were observed, as well as the allelic (AF) and genomic (GF) frequencies (Table 4).

In this study, the GF of the TT gene was higher than the frequency shown in the studies by Pereira et al.[4] and Reuter et al.,[24] but lower than that of the studies by Flores et al.[25] and Xi et al.[26] Regarding the AT gene, the GF was higher than that observed in the other studies shown in Table 4. The AA gene showed lower frequency when compared with the studies by Pereira et al.[4] and Reuter et al.,[24] but was higher than that of the studies by Flores et al.[25] and Xi et al.[26] In relation to the AF of T, a higher frequency was found than that of Pereira et al.[4] and Reuter et al.,[24] and a lower AF for the A allele.

## Discussion

The rs9939609 SNP of the *FTO* gene has been extensively studied in the scientific environment, especially in relation to its influence on the body. Wahlén et al.,[27] studying the association between fat cell metabolism and this SNP, concluded that individuals who are heterozygous (AT) for this polymorphism would have a greater capacity for lipid deterioration due to a high concentration of an organic compound called glycerol. Another relevant finding about this SNP is its possible association with eating habits. It is believed that carriers of the A allele, both in homozygous and heterozygous states, would have a higher preference for fatty foods and little control to avoid their consumption.

In this study, the analyzed SNP was not associated with obesity. Moreover, it is important to emphasize that BMI values were close in relation to the different genotypes (AA, AT, and TT), which may highlight the absence of an association between this genotype and BMI.

The association of this polymorphism with obesity shows quite diverse conclusions in the literature and the frequency is quite varied, according to the assessed ethnic group or even whether the studies are carried out in adult populations, adolescents, or children.

In the study by Pereira et al.,[4] aiming to evaluate the association between the *FTO*, *AKT1,* and *AKTIP* gene polymorphisms and childhood obesity, a sample of Brazilian children was studied, consisting of 195 obese and 153 non-obese individuals, but no association was found between the polymorphisms and obesity/overweight. According to the authors, although several variations of the *FTO* gene have been associated with obesity in populations with a European origin, their effects on other ethnicities remain to be established, and the Brazilian ethnic mixing may be a reason for the lack of association between this polymorphism and obesity.

Also in Brazil, another study pointed to the absence of association between metabolic and anthropometric parameters and *FTO* gene polymorphisms in a sample consisting of children and adolescents. The authors' explanation for this result is associated to the fact that the Brazilian population is mixed and heterogeneous.[13]

However, there are other studies, such as that of Reuter et al.,[24] which found a significant association between the A allele of the rS9939609 SNP of the FTO gene and obese and/or overweight individuals classified using the BMI as the main parameter. Liu et al.[28] found that, irrespective of the sample's place of origin, in this case 289 young European and African-Americans aged 6–19 years, the presence of at least one A allele was directly related to the development of obesity.

Corroborating the present findings, the study by Flores et al.,[25] conducted in Mexico, showed that in addition to the lack of a significant association between genotype and body composition in schoolchildren, both the allelic frequency of A and the genotypic frequency of AA were lower compared to the others, at 13% and 1%, respectively. However, the method used by these researchers for the evaluation of body composition was the absorptiometry technique using DXA.

The use of BMI to evaluate body composition is very common in the literature. In this study, the ADP technique was used to classify obesity, which is considered the gold standard method. It should be noted that this technique shows higher sensitivity and is more robust, classifying a greater number of individuals as obese when compared to BMI.[29]

Body composition varies greatly in adolescents and depends on age, gender, ethnicity, height, and sexual maturation.[30] As shown in Table 4, different prevalence rates of obesity in adolescents can be found in the literature. Thus, the differences in the literature regarding the association between the *FTO* gene and obesity can be explained by the different methods used to classify obesity in adolescents.

The results of this study also indicate that the adolescents showed similar anthropometric measures (BMI, WC, WHtR, %BF), regardless of the genotype. Xi et al.[26] carried out a study with obese and non-obese children and adolescents from Beijing, China, in order to investigate the association between the *FTO* gene polymorphism (rs9939609) with WHtR, WC, %BF, BMI, systolic and diastolic blood pressure, and fasting glycemia, among other associated variables, and found a strong association of the anthropometric measurements with the polymorphism.

In this context, it can be observed how different the findings can be regarding this subject, which leads to different interpretations. One of them refers to the different prevalence rates of the alleles in relation to each population.

The allelic frequencies of the present study were very similar, since in the non-obese group they were 37.43% and 62.57%, whereas in the obese group they were 36.84% and 63.16% for the A and T alleles, respectively. For the whole sample, the frequencies were 37.23% for the A allele and 62.76% for the T allele. This indicates the absence of a possible association between the allelic frequencies and the group to which they belong, categorized by the percentage of body fat.

This is the first study to report data on the prevalence of alleles of this SNP in the population of the Brazilian Northeast, as there are no defined values that represent Brazil, so that a comparison can be made with populations from other countries or continents.

Therefore, the literature indicates that the association of this SNP with obesity can have quite varied results, and also when compared with different anthropometric parameters for obesity classification or body mass increase indicators. Gupta et al.[31] report that the ethnic composition of a population can have a strong influence on the allelic and genotypic frequencies of polymorphisms, leading to the need for studies that use similar methodologies in different populations, aiming to validate the results with robust and reproducible data.

In this sense, as a strong point, this is the first study carried out with adolescents from the Brazilian Northeast, using different anthropometric measures, such as the use of the ADP technique to classify the groups regarding obesity and, therefore, evaluate the association of the rs9939609 polymorphism of the *FTO* gene with obesity. The high cost to perform the study constitutes a weak point.

The analysis of the study data showed there was no association of the rs9939609 polymorphism of the *FTO* gene with the development of obesity, nor there was any difference between the means of BMI, WC, %BF, and WHtR with the different genotypes.

Thus, it is suggested that new studies using the same protocol should be performed, since there are controversies in the literature regarding the frequency of this SNP in relation to the studied ethnic group, as well as the discrepancy of the findings in relation to the age group of the analyzed populations.

## Funding

Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPq and Fundação de Amparo à Pesquisa e ao Desenvolvimento Científico e Tecnológico do Maranhão – FAPEMA.

## Conflicts of interest

The authors declare no conflicts of interest.

## Acknowledgements

The authors are grateful to CNPq, FAPEMA, Hospital Universitário da UFMA, to the Genetics and Molecular Biology Laboratory of UFMA, to the coordination of the RPS Cohort Consortium of São Luís, and to all adolescents who agreed to participate in the study.

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