

## ORIGINAL

## Nutritional Assessment

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## Conflict of interest

The authors declare that there are no conflict of interests.

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# Association between sexual maturation with neck circumference and body mass index in Brazilian schoolchildren

## Associação entre maturação sexual com a circunferência do pescoço e o índice de massa corporal em estudantes brasileiros

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### ABSTRACT

#### Objective

We aimed to evaluate the association of neck circumference and body mass index with sexual maturation in nine-year-old children.

#### Methods

This is a cross-sectional study nested in a Brazilian cohort study named the Predictors of Maternal and Infant Excess Body Weight Study. The present study used data from adult women and their children obtained at baseline and after 2 and 9 years of follow-up. The child's sexual maturation was assessed according to Tanner stage. Logistic regression models adjusting for important covariates were used to examine the association of neck circumference with Tanner stages.

#### Results

The prevalence in stages 2-5 for breast development in girls and for genitalia in boys was 69.1% and 51.3%, respectively. There was a higher ( $p < 0.05$ ) percentage of girls (35.3%) at stages 2-5 for pubic hair development when compared to boys (9.2%). For each unit increase in body mass index and neck circumference, the odds of girls being 2-5 stages for breast development were 1.52 (95% CI 1.17-1.97) and 2.67 (95% CI 1.40-5.09) times, respectively. In other words, the odds of girls being 2-5 stages for breast development were about 1.8 times higher when neck circumference was considered as a predictor, in relation to the body mass index measure (OR=2.67 vs. OR=1.52, respectively).

## Conclusion

Our results revealed that neck circumference, as well as body mass index, is associated with sexual maturation, especially in girls. This is an important result from a public health perspective because, in addition to body mass index, neck circumference may also be used for monitoring sexual maturation in children.

**Keywords:** Body mass index. Children. Puberty. Sexual precocity.

## RESUMO

### Objetivo

*Avaliar a associação da circunferência do pescoço e do índice de massa corporal com a maturação sexual em crianças de nove anos de idade.*

### Métodos

*Trata-se de um estudo transversal alinhado a um estudo de corte brasileiro denominado Preditores do Excesso de Peso Corporal Materno-infantil. O presente estudo utilizou dados de mulheres adultas e seus filhos obtidos no estudo de base e após 2 e 9 anos de acompanhamento. A maturação sexual da criança foi avaliada segundo o estágio de Tanner. Modelos de regressão logística ajustados para importantes covariáveis foram usados para testar a associação da circunferência do pescoço com estágios de Tanner.*

### Resultados

*A prevalência nos estágios 2-5 para desenvolvimento de mamas em meninas, e para genitália em meninos foi de 69,1% e 51,3%, respectivamente. Houve maior ( $p<0,05$ ) percentual de meninas (35,3%) nos estágios 2-5 para desenvolvimento de pelos pubianos quando comparadas aos meninos (9,2%). Para cada aumento de uma unidade do índice de massa corporal e da circunferência do pescoço, as chances de as meninas apresentarem estágios 2-5 para desenvolvimento de mamas foram de 1,52 (95% IC 1,17-1,97) e 2,67 (95% IC 1,40-5,09) vezes, respectivamente. Ou seja, as chances de as meninas apresentarem estágios 2-5 para desenvolvimento da mama foram cerca de 1,8 vezes maiores quando a circunferência do pescoço foi considerada como preditor, em relação a medida do índice de massa corporal (OR=2,67 vs. OR=1,52, respectivamente).*

### Conclusão

*Este estudo revelou que a circunferência do pescoço e o índice de massa corporal foram associados à maturação sexual em meninas. Este é um resultado importante do ponto de vista da saúde pública visto que a circunferência do pescoço, adicionalmente ao índice de massa corporal, pode ser uma medida complementar para monitorar a maturação sexual em crianças.*

**Palavras-chave:** Índice de massa corporal. Crianças. Puberdade. Precocidade sexual.

## INTRODUCTION

Sexual maturation is a period characterized by changes in the organism that occur rapidly during puberty in both boys and girls [1]. During this period, several changes occur in the development of children, which promote maturation of the gonads and the ability to reproduce [2]. The process of sexual maturation comprises a set of actions triggered by reactivation of the Hypothalamic-Pituitary-Gonadal (HPG) axis that develops during the fetal period [3]. In the next three months of life, HPG reactivates, a period known as mini-puberty, followed by another reactivation around 8-9 years of age [3].

Sexual maturation is influenced by several factors, including genetics, sex, ethnicity, and environmental and nutritional factors [4]. Indeed, overweight and obesity can induce the anticipation of the sexual maturation stage and exert important effects throughout the life of these individuals [5]. In girls, mammary development during sexual maturation is associated with the formation of subcutaneous and visceral adipose tissue [6]. In addition, overweight girls exhibit a more pronounced reduction in the median age of Tanner stages over the years, whereas in boys, this reduction occurs regardless of weight status [7]. Thus, monitoring the nutritional status of children throughout

their development also helps monitor their pubertal development. The main tool to assess sexual maturation is the Sexual Maturity Classification proposed by Marshall and Tanner in the 1940s, which evaluates the development of the external genitalia: testicle volume in boys, breasts in girls, and pubic hair in both sexes [8]. Since sexual maturation involves psychological, behavioral, and nutritional issues, nutritional assessment is essential to monitor and understand the stages of child development [9].

Among the different parameters used to assess nutritional status, the Body Mass Index (BMI) is still the main parameter used [10]. However, BMI does not provide information about body fat composition [11]. Parameters that assess body fat, such as waist, arm and neck circumferences, are more appropriate because they also indicate cardiovascular risk, metabolic syndrome, changes in glucose metabolism, among others, which contribute to mapping negative health outcomes [11,12]. Among the parameters that assess body fat, Neck Circumference (NC) has been highlighted in the last decade since it is a reliable, practical and low-cost measure [10,13].

We found no studies associating NC with sexual maturation during the pre-adolescent period. Therefore, the present study aimed to evaluate the association of NC and BMI with sexual maturation in nine-year-old children.

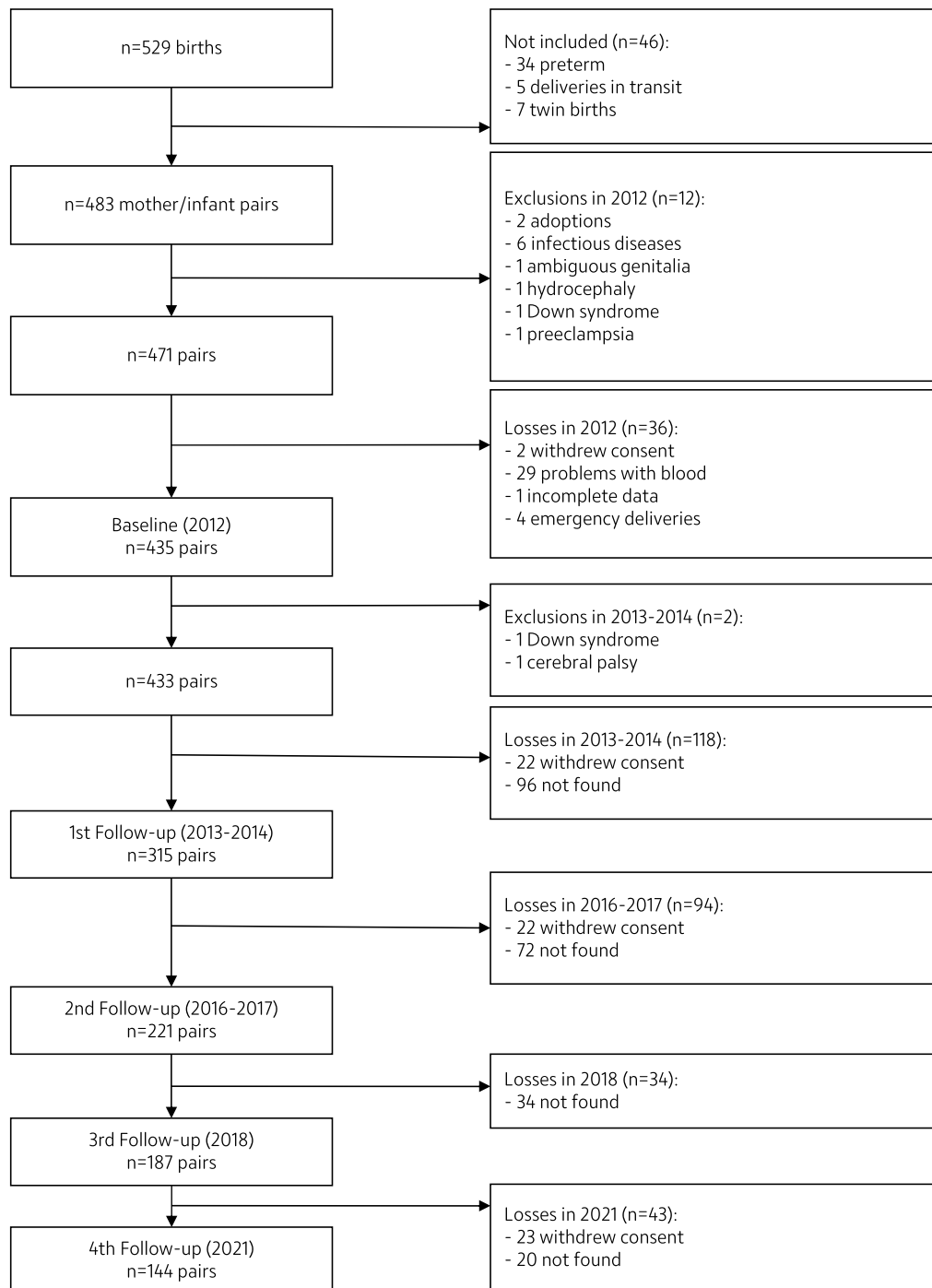
## METHODS

We conducted a cross-sectional study nested in a cohort study named the Predictors of Maternal and Infant Excess Body Weight (PREDI) Study. The PREDI Study was started in 2012 in a public maternity hospital in Joinville, in the State of Santa Catarina, Brazil.

Details of the PREDI Study recruitment process have been described previously [10,14]. In summary, all women over the age of 18 years, who gave birth to a full-term singleton (between 37 and 42 weeks of gestation), were invited to participate in the study with their children at baseline. Exclusion criteria were plans for adoption immediately after delivery and the presence of an infectious contagious disease (acquired immune deficiency syndrome, hepatitis, syphilis, and toxoplasmosis), birth defects, Down syndrome, and preeclampsia. Of the 529 eligible mother-child pairs, 435 participated at baseline in 2012, 315 at 1<sup>st</sup> follow-up (2013-14), 221 at 2<sup>nd</sup> follow-up (2016-17), 187 at 3<sup>rd</sup> follow-up (2018), and 144 at 4<sup>th</sup> follow-up (2021) (Figure 1).

All follow-ups were conducted in the homes of the participants, and all mothers and their children of the previous follow-up were invited to participate in the subsequent follow-up. A trained health team collected the data in the maternity hospital and the participant's home using a previously tested structured questionnaire. Details of the data collection tools have been described previously [10,14].

The present study used data from baseline (birth weight, gender, type of delivery, pre-pregnancy BMI, and Gestational Weight Gain [GWG]), and from the 1<sup>st</sup> (duration of breastfeeding) and 4<sup>th</sup> (child's BMI, maternal age, maternal education, marital status, monthly household income, child's NC, and sexual maturation) follow-ups. At baseline, the mothers received information about the study within 48 hours after the birth of their offspring. If both the mother and her child met the study's inclusion criteria, they were invited to participate by providing informed consent according to the Ethics Committee of the Universidade da Região de Joinville [14]. Once enrolled in the study, the mothers completed a previously tested structured questionnaire that included anthropometric measurements and clinical, biological, demographic, and socioeconomic data [14]. The questionnaire was administered in the room of a private maternity hospital within 48 hours after delivery and



**Figure 1** – Flow diagram of the PREDI cohort study, Joinville, Brazil, 2012–2021.

Source: Adapted from [30].

immediate maternal postpartum height was assessed on that occasion. Immediate postpartum height was measured to the nearest 0.1 cm using a portable stadiometer (WCS®, Compact Model, Curitiba, Brazil) on a wall without skirting [14]. The mothers stood in an orthostatic position wearing light clothing and no shoes and their weight was evenly distributed.

Pre-pregnancy BMI ([weight (kg)/height (m<sup>2</sup>)]) was calculated based on the mothers' self-reported pre-pregnancy weight and immediate postpartum measured height. Pre-pregnancy

weight was classified according to the World Health Organization BMI cut-offs, [15] which classifies women with a BMI  $<18.5 \text{ kg/m}^2$  as underweight, between 18.5 and  $24.9 \text{ kg/m}^2$  as normal weight, between 25 and  $29.9 \text{ kg/m}^2$  as overweight, and  $\geq 30.0 \text{ kg/m}^2$  as obese. The GWG was obtained by subtracting pre-pregnancy weight from the weight at delivery (measured on the day before delivery in the maternity hospital). The adequacy of GWG was assessed according to the 2009 Institute of Medicine guidelines [16].

The child's birth weight and length were collected from the hospital records. Birth weight was classified into three categories according to gestational age and sex: small for gestational age (SGA;  $<10^{\text{th}}$  percentile), adequate for gestational age (AGA; 10-90<sup>th</sup> percentile), and large for gestational age (LGA;  $>90^{\text{th}}$  percentile) according to the INTERGROWTH-21<sup>st</sup> Project [17]. Breastfeeding duration (in months) was self-reported by the mothers in the 1<sup>st</sup> follow-up.

In the 4<sup>th</sup> follow-up, the child's weight was measured on a digital scale (G-Tech®, Glass 7 Model, Zhongshan, China) with a capacity of 180 kg to the nearest 0.1 kg, with the child wearing light clothing and no shoes or accessories (jewelry, watches, coats). Height was measured to the nearest 0.1 cm using a portable ultrasonic digital stadiometer (AvaNutri®, CAVA-040, Rio de Janeiro, Brazil) [14]. The measurements were taken according to the Brazilian Guidelines for Collection and Analysis of Anthropometric Data in Health Services. The children's nutritional status was divided into two categories based on the 2007 World Health Organization Growth Reference for School-aged Children and Adolescents for BMI-for-age and sex:  $\leq 85^{\text{th}}$  percentile and  $> 85^{\text{th}}$  percentile [18]. The NC was measured with a 150-cm flexible tape to the nearest 1 mm. The children were standing and the measurement was obtained at the level of the thyroid cartilage, with the tape not compressing the skin [10]. All anthropometric measurements were performed in duplicate and the mean of the two measurements was used for analysis.

The child's sexual maturation data were obtained using the printed scales of the Brazilian Society of Pediatrics [19] and classified according to the criteria proposed by Tanner [8]. The mothers received information about the Tanner criteria and the importance of the assessment. A researcher then asked the mother to point out the stage of development of her child on the printed scale. The scales included line drawings of each Tanner stage: genital development for boys (Tanner G1-G5), breast development for girls (Tanner B1-B5), and pubic hair development for boys and girls (Tanner P1-P5) [8].

Data were analyzed using IBM®SPSS® Statistics for Macintosh, version 27.0 (Released 2020, IBM Corp, Armonk, NY). To examine differences between the mother-child pairs enrolled at baseline and those not enrolled in the 4<sup>th</sup> follow-up, maternal education, marital status, birth weight, and gender were compared using the Student *t*-test and the chi-square test for continuous and categorical variables, respectively (Table 1).

Due to the small number of individuals in each category, the children's Tanner stage was divided into two categories: stage 1 and stages 2-5. The chi-square test was applied to compare the prevalence of categorical variables according to the child's Tanner stage (stage 1 vs. stages 2-5; Table 2). The Mann-Whitney U test was applied to compare the median and interquartile range (IQR) of BMI and NC from the 1<sup>st</sup> to the 4<sup>th</sup> follow-up according to child's Tanner stage (Table 2).

Odds Ratios (OR) and 95% Confidence Intervals (CI) were calculated using logistic regression to investigate the association of BMI and NC with Tanner stages (reference category: stage 1; risk category: stages 2-5) and other risk factors. Each exposure was examined separately in Model 1 and two exposures were not entered at once (Table 3). Covariates from Table 2 with  $p < 0.10$  (results not

shown in Table 2: GWG, marital status, monthly household income, BMI and NC) were selected for inclusion in the adjusted models in order to identify independent determinants of Tanner stage. The variable gender was only considered in models 2 and 3 for pubic hair development (Table 3).

The goodness-of-fit of the models was assessed using the -2 Log-likelihood value, with lower values indicating better fits. A  $p$ -value  $<0.05$  was considered statistically significant in all analyses.

This study was conducted in accordance with the guidelines established in the Declaration of Helsinki and all procedures involving humans were approved by the Review and Ethics Committee of the Universidade da Região de Joinville (CAAE: 40242620.4.0000.5366). Written informed consent was obtained from all participants included in the study.

**Table 1** – Losses to follow-up: from baseline to fourth follow-up. PREDI Study, Joinville, Brazil, 2012–2021.

Continuous variables	Participants in 4 <sup>th</sup> follow-up (n=144)	Losses to follow-up from baseline (n=291)	p
	Mean (SD)	Mean (SD)	
Maternal education (years)	9.6 (2.9)	9.3 (3.1)	0.348*
Birth weight (g)	3.4 (0.4)	3.4 (0.5)	0.207*
Categorical variables	n (%)	n (%)	p
Marital status			0.223**
Married/consensual union	124 (34.3)	237 (65.7)	
Other	20 (27.0)	54 (73.0)	
Gender			0.924**
Boys	76 (32.9)	155 (67.1)	
Girls	68 (33.3)	136 (66.7)	

Note: \*Student t-test; \*\*X<sup>2</sup> test. SD: Standard Deviation.

**Table 2** – Characteristics of the study participants according to the child's sexual maturation (n=144). The PREDI Study, Joinville, Brazil, 2021.

1 of 2.

Variables	Sexual Maturation								
	B1 (n=21)	B2-B5 (n=47)	Total (n=68)	G1 (n=37)	G2-G5 (n=39)	Total (n=76)	P1 (n=113)	P2-P5 (n=31)	Total (n=144)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
<b>Categorical variables*</b>									
<b>Children</b>									
Birth weight									
SGA/AGA	16 (31.4)	35 (68.6)	51 (75.0)	30 (50.0)	30 (50.0)	60 (78.9)	88 (79.3)	23 (20.7)	111 (77.1)
LGA	5 (29.4)	12 (70.6)	17 (25.0)	7 (43.8)	9 (56.3)	16 (21.1)	25 (75.8)	8 (24.2)	33 (22.9)
Gender									
Boys				37 (48.7)	39 (51.3)	76 (100.0)	69 (90.8)	7 (9.2)	76 (52.8)
Girls	21 (30.9)	47 (69.1)	68 (100.0)				44 (64.7)	24 (35.3)*	68 (47.2)
Duration of breastfeeding (months)									
≥ 6	8 (32.0)	17 (68.0)	25 (36.8)	12 (50.0)	12 (50.0)	24 (32.0)	38 (77.6)	11 (22.4)	49 (34.3)
< 6	13 (30.2)	30 (69.8)	43 (63.2)	24 (47.1)	27 (52.9)	51 (68.0)	74 (78.7)	20 (21.3)	94 (65.7)
BMI (percentile)									
≤ 85 <sup>th</sup>	21 (38.9)	33 (61.1)	54 (79.4)	22 (43.1)	29 (56.9)	51 (67.1)	83 (79.0)	22 (21.0)	105 (72.9)
> 85 <sup>th</sup>	0	14 (100.0)*	14 (21.6)	15 (60.0)	10 (40.0)	25 (32.9)	30 (76.9)	9 (23.1)	39 (27.1)
<b>Mother</b>									
Age (years)									
<30	1 (50.0)	1 (50.0)	2 (2.9)	3 (60.0)	2 (40.0)	5 (6.6)	5 (71.4)	2 (28.6)	7 (4.9)
30–40	14 (37.8)	23 (62.2)	37 (54.4)	21 (47.7)	23 (52.3)	44 (57.9)	66 (81.5)	15 (18.5)	81 (56.2)
≥40	6 (20.7)	23 (79.3)	29 (42.6)	13 (48.1)	14 (51.9)	27 (35.5)	42 (75.0)	14 (25.0)	56 (38.9)
Education (years)									
≥12	12 (40.0)	18 (60.0)	30 (46.1)	19 (48.7)	20 (51.3)	39 (52.0)	50 (72.5)	19 (27.5)	69 (49.3)
9–12	4 (21.1)	15 (78.9)	19 (29.2)	12 (46.2)	14 (53.8)	26 (34.7)	37 (82.2)	8 (17.8)	45 (32.1)
<9	3 (18.8)	13 (81.3)	16 (24.6)	5 (50.0)	5 (50.0)	10 (13.3)	23 (88.5)	3 (11.5)	26 (18.6)
Marital status									
Married/consensual union	10 (23.3)	33 (76.7)	43 (65.2)	26 (51.0)	25 (49.0)	51 (68.0)	70 (74.5)	24 (25.5)	94 (66.7)
Other	10 (43.5)	13 (56.5)	23 (34.8)	10 (41.7)	14 (58.3)	24 (32.0)	41 (87.2)	6 (12.8)	47 (33.3)

**Table 2** – Characteristics of the study participants according to the child's sexual maturation (n=144). The PREDI Study, Joinville, Brazil, 2021.

2 of 2.

Variables	Sexual Maturation								
	B1 (n=21)	B2-B5 (n=47)	Total (n=68)	G1 (n=37)	G2-G5 (n=39)	Total (n=76)	P1 (n=113)	P2-P5 (n=31)	Total (n=144)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Monthly household income (MW)									
≥5	1 (6.7)	14 (93.3)	15 (23.4)	10 (45.5)	12 (54.5)	22 (30.1)	27 (73.0)	10 (27.0)	37 (27.0)
3-5	13 (38.2)	21 (61.8)	34 (53.1)	19 (61.3)	12 (38.7)	31 (42.5)	52 (80.0)	13 (20.0)	65 (47.4)
<3	5 (33.3)	10 (66.7)	15 (23.4)	6 (30.0)	14 (70.0)	20 (27.4)	29 (82.9)	6 (17.1)	35 (25.5)
Type of delivery									
Vaginal	16 (35.6)	29 (64.4)	45 (66.2)	22 (43.1)	29 (56.9)	51 (67.1)	78 (81.3)	18 (18.8)	96 (66.7)
Cesarean section	5 (21.7)	18 (78.3)	23 (33.8)	15 (60.0)	10 (40.0)	25 (32.9)	35 (72.9)	13 (27.1)	48 (33.3)
Pre-pregnancy BMI (kg/m <sup>2</sup> )									
< 25	16 (36.4)	28 (63.3)	44 (64.7)	25 (52.1)	23 (47.9)	48 (63.2)	72 (78.3)	20 (21.7)	92 (63.9)
≥ 25	5 (20.8)	19 (79.2)	24 (35.3)	12 (42.9)	16 (57.1)	28 (36.8)	41 (78.8)	11 (21.2)	52 (36.1)
Gestational weight gain									
Appropriate	11 (26.8)	30 (73.2)	41 (60.3)	26 (59.1)	18 (40.9)	44 (57.9)	63 (74.1)	22 (25.9)	85 (59.0)
Excessive	10 (37.0)	17 (63.0)	27 (39.7)	11 (34.4)	21 (65.6)*	32 (42.1)	50 (84.7)	9 (15.3)	59 (41.0)
Continuous variables**									
BMI (kg/m <sup>2</sup> ); Median (IQR)	15.4 (3.0)	18.9 (5.0)*	18.1 (5.0)	17.9 (7.0)	17.3 (5.0)	17.5 (6.0)	17.3 (5.0)	18.4 (5.0)	17.5 (5.0)
Neck circumference (cm); Median (IQR)	26.5 (1.0)	28.5 (2.4)*	27.6 (2.7)	28.9 (5.4)	28.6 (2.4)	28.8 (3.5)	28.2 (3.3)	28.4 (2.6)	28.3 (3.2)

Note: \*Chi-square test; \*\*Mann-Whitney U test. \* $p < 0.05$ . AGA: Appropriate for Gestational age; B: Breast Development; BMI: Body Mass Index; G: Genitalia Development; IQR: Interquartile Range; LGA: Large for Gestational Age; MW: Minimum Wage (1 MW=US\$ 207.00 in 2021); P: Pubic hair Development; SGA: Small for Gestational Age.

## RESULTS

There was no significant difference in maternal education, marital status, birth weight or gender between mothers/children enrolled at baseline and those considered losses in the 4<sup>th</sup> follow-up (Table 1).

Table 2 shows the characteristics of the study participants according to the Tanner classification. The prevalence of girls at Tanner stages B2-B5 and boys at G2-G5 was 69.1% and 51.3%, respectively. There was a higher prevalence of boys at stages G2-G5 whose mothers had excessive GWG (65.6%) when compared to boys whose mothers had appropriate GWG. Regarding Tanner pubic hair classification, there was a significantly ( $p < 0.05$ ) higher percentage of girls at stages P2-P5 (35.3%) when compared to boys (Table 2). Regarding anthropometric measures, the Mann-Whitney test showed significantly ( $p < 0.05$ ) higher median and IQR of BMI and NC at stages B2-B5 compared to stage B1; 18.9 (5.0) kg/m<sup>2</sup> vs. 15.4 (3.0) kg/m<sup>2</sup> and 28.5 (2.4) cm vs. 26.5 (1.0) cm, respectively, for BMI and NC. However, there was no significant difference between median BMI or NC in the Tanner G and P classifications (Table 2).

Table 3 shows the results of logistic regression analyses of sexual maturation considering BMI and NC. In the unadjusted analyses, BMI and NC were significantly associated with Tanner B stage (Table 3, Model 1). For each unit increase in BMI and NC, the odds of girls being stages B2-B5 were 1.52 and 2.67 times, respectively (Table 3, Model 1). The GWG and gender were associated with Tanner G and P stages, respectively (OR=2.76, 95% CI 1.07-7.10,  $p = 0.035$  for GWG; OR=5.38, 95% CI 2.14-13.53,  $p < 0.001$  for gender; Table 3, Model 1). Furthermore, girls were more likely to develop Tanner stages P2-P5 at 9 years of age when compared to boys of the same age (OR=6.03, 95% CI 2.32-15.63,  $p < 0.001$  for BMI, Model 2; OR=6.57, 95% CI 2.40-17.93,  $p < 0.001$  for NC, Model 3) (Table 3).



**Table 3** – Logistic regression models for stages 2-5 of sexual maturation of children at age 9 years. The PREDI Study, Joinville, Brazil, 2021.

Variables	Model 1	<i>p</i>	Model 2	<i>p</i>	Model 3	<i>p</i>
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
Breast						
Body mass index (kg/m²)	1.52 (1.17-1.97)	0.002	1.52 (1.17-1.97)	0.002		
Neck circumference (cm)	2.67 (1.40-5.09)	0.003			2.67 (1.40-5.09)	0.003
Gestational weight gain						
Appropriate	Reference					
Excessive	0.62 (0.22-1.77)	0.374				
Marital status						
Married/consensual union	Reference					
Other	0.39 (0.13-1.16)	0.093				
Monthly household income	1.42 (0.95-2.11)	0.087				
Genitalia						
Body mass index (kg/m2)	0.92 (0.82-1.04)	0.174	0.92 (0.82-1.04)	0.202		
Neck circumference (cm)	0.91 (0.76-1.09)	0.331			2.83 (1.09-7.36)	0.292
Gestational weight gain						
Appropriate	Reference		Reference		Reference	
Excessive	2.76 (1.07-7.10)	0.035	2.72 (0.99-7.01)	0.041	2.83 (1.09-7.36)	0.033
Marital status						
Married/consensual union	Reference					
Other	1.46 (0.55-3.88)	0.452				
Monthly household income	0.98 (0.77-1.25)	0.858				
Pubic hair						
Body mass index (kg/m²)	1.05 (0.95-1.17)	0.125	1.09 (0.97-1.22)	0.125		
Neck circumference (cm)	0.99 (0.83-1.17)	0.870			1.13 (0.92-1.38)	0.240
Gestational weight gain						
Appropriate	Reference					
Excessive	0.51 (0.22-1.22)	0.131				
Marital status						
Married/consensual union	Reference					
Other	0.43 (0.16-1.13)	0.087				
Monthly household income	1.07 (0.87-1.32)	0.520				
Gender						
Boys	Reference		Reference		Reference	
Girls	5.38 (2.14-13.53)	<0.001	6.03 (2.32-15.63)	<0.001	6.57 (2.40-17.93)	<0.001

Note: Model 1: Unadjusted model; Model 2: Adjusted model considering body mass index; Model 3: Adjusted model considering neck circumference. The variable gender was only considered in models 2 and 3 for pubic hair development. Except for neck circumference and body mass index, the results of the adjustment variables were only included in model 2 and 3 when  $p < 0.05$ . OR: Odds Ratio; CI: Confidence Interval.

## DISCUSSION

In the present study the results revealed that BMI and NC were associated with breast development, with higher median values of BMI and NC in stages 2-5. Furthermore, using the CP measurement as a predictor of breast sexual maturation showed higher odds of girls presenting stages 2-5 when compared to the BMI measurement.

The association between sexual maturation stages and body weight is well documented in the literature [6]. However, we did not find studies that have associated sexual maturation and body weight using NC. Nevertheless, our results agree with other studies that investigated the relationship between BMI and sexual maturation in children [7,9].

The BMI is still the main measure used to assess the nutritional status of individuals in any age group [20]. However, some authors have reported divergent results, especially for boys [21]. A study carried out in Norway with boys aged 6-16 years revealed that only low weight (BMI z score < -1) was associated with changes in sexual maturation [21]. In Bulgaria, a study that investigated 4,030 boys aged between 7 and 19 years found a delay in pubertal development stages in boys with low BMI (< 12<sup>th</sup> percentile), while an earlier onset of puberty was observed in boys with BMI > 85<sup>th</sup> percentile [22].



Although BMI is an indicator commonly associated with sexual maturation, it does not assess adiposity [23]. The BMI is the ratio between weight and height that does not determine adiposity. Weight is a measure of mass in Newtons converted into kilograms that expresses the force exerted through gravity [24], while height is a measure of length. These parameters are therefore not effective in assessing body composition [12]. Indeed, adiposity can be correctly evaluated when circumference measurements are used, such as arm, waist and neck circumference [9,25]. The use of circumference measurements permits to assess the distribution of body fat, which predicts individual health risks regardless of weight, height or age group [10,26]. Among the different circumference measurements available, NC seems to be an excellent parameter for evaluating the association with sexual maturation not only because it assesses adiposity but also because it is a practical method that does not require removal of the individual's clothing and uses only a measuring tape, among other advantages [10,12,13,26].

Sexual maturation is a physiological process characterized by the release of steroid hormones, mainly testosterone in boys and estradiol in girls, which are responsible for the morphological changes that occur during the pubertal period [2]. Mammary development during sexual maturation influences the formation of subcutaneous adipose tissue and visceral tissue in girls [6]. Also, the relationship between adiposity and sexual maturation is well established; adiposity is a measure of body fat and is therefore intrinsically associated with the hormonal flow [6]. Among adipose tissue-related hormones, leptin, luteinizing hormone) and follicle-stimulating hormone seem to affect the pubertal period [27]. Higher leptin levels in obese children trigger early pubertal onset [28]. The effect of leptin concentration on sexual maturation also appears to be influenced by sex [29]. We found a higher percentage (almost eight times) of girls being Tanner P2-P5 stages when compared to boys of the same age, even after adjustment for other covariates, in agreement with other authors [5]. In fact, the gonadotropic secretion responsible for the release of luteinizing hormone and follicle-stimulating hormone can be stimulated by high insulin levels, affecting the production of sex hormone-binding globulin and consequently triggering sexual maturation and early pubertal development [29].

The assessment of sexual maturation is important for monitoring the proper development of the child during a period of intense hormonal flow. An adequate, easy, and accurate indicator that permits to complement the assessment of sexual maturation is essential to ensure the quality of the assessment. Within this context, the use of NC as a complementary measure to monitor puberty in boys and girls seems to be promising and should be further investigated, especially because this parameter also predicts adiposity.

This study has several strengths. First, data came from a birth cohort study and are primary data, a fact providing opportunities for future research in this field. Second, all data including the anthropometric measures were collected using the same equipment and by most members of the same research group, which reduces possible biases. Finally, the possibility of adjustments for potential confounding factors is another strength of the study.

However, some limitations of this study must also be mentioned. First, the pandemic situation of COVID-19 may have contributed to the refusal of some families to continue participation in the study. Second, our results came from a relatively small cohort of mothers and their children living in Brazil; therefore, caution is necessary when comparing the results to other populations. Finally, the lack of a Brazilian reference standard for NC in children impaired analysis of the individuals according to risk group.

## CONCLUSION

In conclusion, our findings showed that NC and BMI were associated with sexual maturation in children at age 9 years. The results are important from a public health perspective since NC, in addition to BMI, enables easy monitoring of sexual maturation in children.

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