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Revista de Saúde Pública

Effect of early determinants on adolescent fat-free mass: RPS cohort of São Luís – MA

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ABSTRACT

OBJECTIVE: To analyze the effects of early determinants on adolescent fat-free mass.

METHODS: A cohort study with 579 adolescents evaluated at birth and adolescence in a birth cohort in São Luís, Maranhão. In the proposed model, estimated by structural equation modeling, socioeconomic status (SES) at birth, maternal age, pregestational body mass index (BMI), gestational smoking, gestational weight gain, type of delivery, gestational age, sex of the newborn, length and weight at birth, adolescent socioeconomic status, "neither study/nor work" generation, adolescent physical activity level and alcohol consumption were tested as early determinants of adolescent fat-free mass (FFM).

RESULTS: A higher pregestational BMI resulted in higher FFM in adolescence (Standardized Coefficient, SC = 0.152; $p < 0.001$). Being female implied a lower FFM in adolescence (SC = -0.633; $p < 0.001$). The negative effect of gender on FFM was direct (SC = -0.523; $p < 0.001$), but there was an indirect negative effect via physical activity level (SC = -0.085; $p < 0.001$). Women were less active ($p < 0.001$). An increase of 0.5 kg (1 Standard Deviation, SD) in birth weight led to a gain of 0.25 kg/m² (0.106 SD) in adolescent FFM index ($p = 0.034$). Not studying or working had a negative effect on the adolescent's FFM (SC = -0.106; $p = 0.015$). Elevation of 1 SD in the adolescent's physical activity level represented an increase of 0.5 kg/m² (0.207 SD) in FFM index ($p < 0.001$).

CONCLUSIONS: The early determinants with the greatest effects on adolescent FFM are gender, adolescent physical activity level, pregestational BMI, birth weight and belonging to the "neither-nor" generation.

DESCRIPTORS: Adolescent Health. Fetal Development. Body Composition. Biological Factors. Social Determinants of Health. Socioeconomic Factors.

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INTRODUCTION

According to the developmental origin of health and disease theory, events occurring during early developmental phases starting from fetal life may be related to determined lifelong health and disease patterns[1]. The prenatal period may influence the distribution of body composition components throughout life, also being affected by maturation and aging, as well as other factors such as diseases and behavioral characteristics[2,3].

Many studies have focused on early determinants as predictors of future body fat, but few have verified the effect of these determinants on fat-free mass (FFM) during different stages of life[3]. Fat-free mass is a clinical indicator of health and a determinant of functional capacity, being associated with a longer survival of patients with heart disease and cancer, among others[4–6]. Its conservation is important for survival during aging[7]. Contemporary aspects related to lifestyle such as physical activity and eating habits have been well established as factors influencing the FFM of an individual[8–10]. However, earlier aspects such as growth during gestation, childhood and adolescence have been investigated, although the available scientific literature is scarce and controversial[3,11].

The major early determinants of FFM at the beginning of adult age are weight and length at birth, as well as maternal (height, socioeconomic conditions and educational level) and gestational (gestational age, pre-gestational weight, smoking during pregnancy) variables[3]. A low birth weight (BW) is associated with a smaller FFM during adulthood, contributing to the risk of sarcopenia and functional disability at the end of life[12], whereas a greater BW may be associated with a greater FFM (especially in men) at 60-64 years[11]. However, it is still unknown whether the effects previously observed on body composition reflect a totally intrauterine programming. There may be confusion due to lifestyle or genetics, in addition to possible pathways mediated by other exposures, which would represent a problem[13].

Also, most of the available evidence has used body mass index (BMI) to assess nutritional status although studies using this tool cannot elucidate whether the associations reflect the influence of growth on fat mass (FM), on FFM, or on both[11]. Furthermore, a systematic review observed that the studies use linear regression for statistical analysis[3]. There is criticism in the literature regarding linear regression since it only investigates direct relationships between the explanatory variables and the outcome, without evaluating the effects of indirect pathways through the mediating variables[14,15].

Understanding the effects of early determinants of future FFM and how body composition behaves over the years using methods that can detect differences between body composition compartments regarding a birth cohort and appropriate statistical analysis is of fundamental importance for the elaboration of public health strategies to promote health and prevent disorders related to reduced FFM.

Thus, the objective of this study was to answer the following questions: what are the major early determinants of FFM in adolescence? Do birth-related factors have a greater effect on FFM during adolescence than factors related to adolescence itself? Are all effects direct or they occur through mediating variables?

METHODS

This was a cohort study based on individuals born in the city of São Luís, Maranhão, Brazil, involving three different periods. This cohort is included in the study "Life-long determinants of obesity, precursors of chronic disease, human capital, and mental health" conducted by the RPS consortium with the Universidade Federal do Maranhão (UFMA), Faculdade de Medicina de Ribeirão Preto (USP), and Universidade Federal de Pelotas (UFPel).

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In São Luís, the subjects of this cohort were evaluated in three phases of life: at birth, in childhood (7 to 9 years) and currently in adolescence (18/19 years). Our study used data collected in the first and third phases of the cohort in the city of São Luís. Initially, the study was conducted in ten public and private hospitals from March 1997 to February 1998. The study sample base included 96.3% of births, excluding non-hospital births and births that occurred in hospitals where fewer than 100 deliveries occurred per year. One in seven births at each maternity hospital was recruited for the study, with proportional sharing of the number of births in each unit. The interviews were conducted at the hospital or at home, and data were collected using the Birth and Interview Recording Card, the Standardized Questionnaire, and the Mortality Investigation Card[16]. We included 2,541 births, with 5.8% loss due to refusal or early discharge.

All subjects included in the first phase were located in the four Military Enlistment branches of São Luís, in the school census of 2014 and in universities. Printed and virtual advertising material, radio and TV networks and social media including WhatsApp and a site especially set up for this purpose were used for dissemination. The subjects identified (n = 684) were invited to attend follow-up. The evaluation focused on outcomes related to nutrition, body composition, precursor factors for chronic diseases, mental health, and human capital (schooling, income and cognitive skills).

The study was conducted with 684 adolescents that were evaluated at birth and during adolescence. Exclusion criteria were twins, subjects who were not born in São Luís and subjects who had no FFM or height data, which were necessary for the construction of the outcome variable. Thus, the final sample consisted of 579 adolescents of both sexes (18/19 years).

Data from the third phase were collected by properly trained students and health graduates. A pilot study was carried out with simulation of all stages of the research, for checking and technical adjustments. Questionnaires used in the study were validated but no reproducibility analysis was carried out. Data were collected in sequentially organized stations including different questionnaires (with questions about socioeconomic, personal and family data, health, physical activity, leisure, sedentary behavior and life habits) and evaluation instruments such as BodPod and densitometry (DEXA).

The DEXA station (Dual Energy X-Ray Absorptiometry) was equipped with a Lunar Prodigy GE Healthcare® model for the measurement of body components and for the estimate of localized fat percent. This machine requires about 15 minutes for whole body scanning and 3 minutes for the examination of each bone density site. The participants were instructed to wear standard clothing, a swimming cap and to remove any accessories. They were previously weighed and measured and then positioned for the measurements of whole-body composition and of lumbar spine and femoral head bone mass. The instrument also provided the measurement of FM and FFM of each adolescent. Data collection and entry were performed using the Research Electronic Data Capture (RedCap).

In the theoretical model proposed, the variables of mother and newborn, as well as the variables of the adolescents, determine the FFM of the adolescent. The socioeconomic status at birth and during adolescence represents latent variables constructed from other variables observed. All the other variables were observed (Figure 1). The socioeconomic status (SES) construct for both birth and adolescence was derived from the variables schooling of the family head (at birth and adolescence – never studied, 1 to 4 years, 5 to 8 years, 9 to 11 years, and 12 or more years of study) and monthly family income (birth and adolescence – minimum wages (MW); the national minimum wage was R$120.00 in 1997 and R$ 880.00 in 2016: ≤1; 1.1 to 1.9; 2 to 2.9; 3 to 4.9; 5 to 9.9, and ≥10).

The main explanatory variables were birth weight and level of physical activity of the adolescent. Birth weight (kg) was recorded in a continuous manner in the model. The level of physical activity was determined using the 24-h Physical Activity recall survey elaborated

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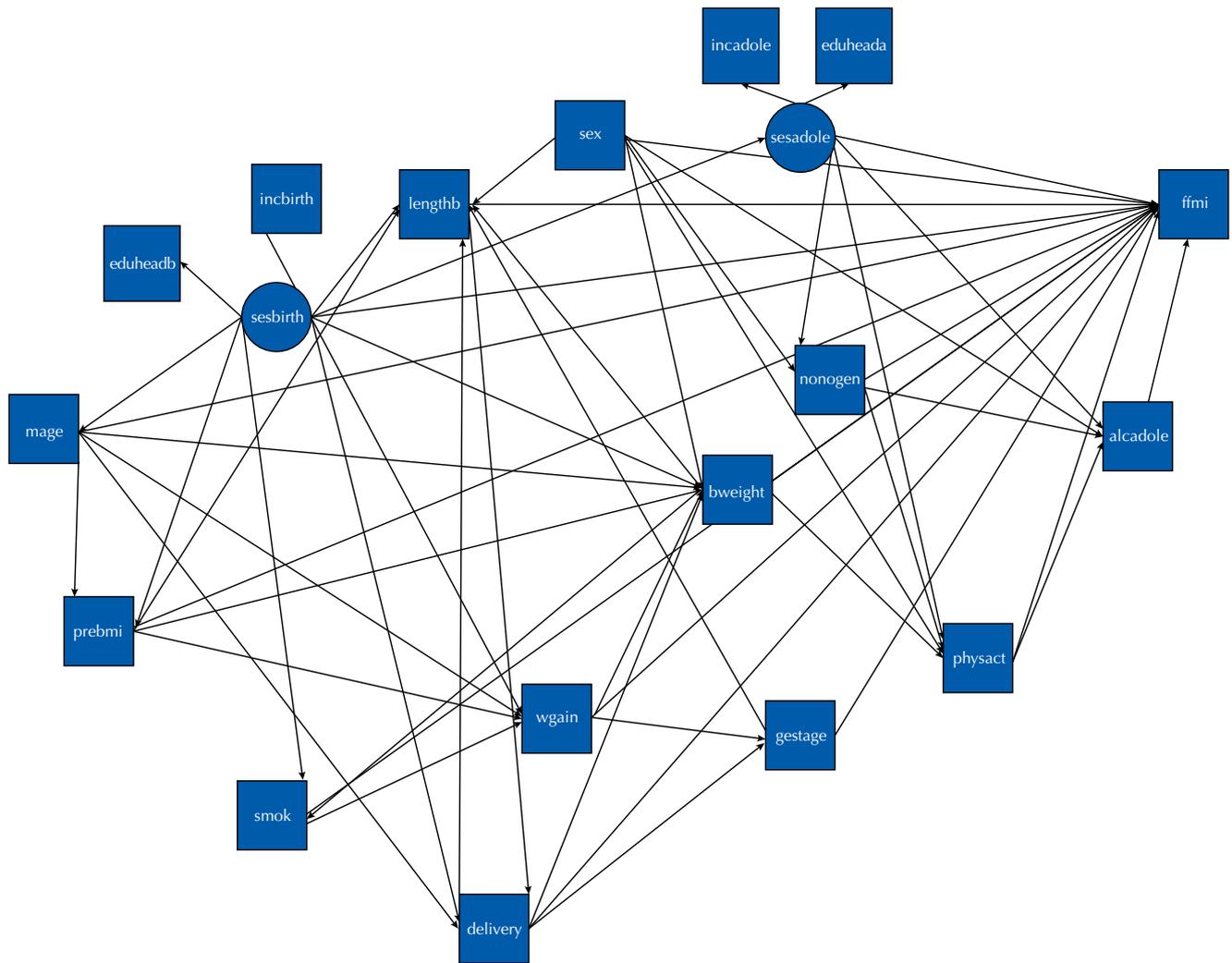
eduheadb: schooling of family head at birth; **incbirth**: monthly family income in minimum wages; **sesbirth**: socioeconomic status at birth; **mage**: maternal age; **prebmi**: pregestational BMI; **smok**: smoking during pregnancy; **wgain**: gestational weight gain; **delivery**: type of delivery; **sex**: sex of the newborn; **lengthb**: birth length; **bweight**: birth weight; **eduheada**: schooling of family head during adolescence; **incadole**: monthly family income in minimum wages during adolescence; **sesadole**: socioeconomic status of the adolescent; **nonogen**: "neither-nor" generation"; **physact**: level of physical activity of the adolescent; **alcadole**: alcohol consumption by the adolescent; **ffmi**: fat-free mass index of the adolescent.

Figure. Theoretical model of the associations of observed and latent variables with the fat-free mass of adolescents of the RPS cohort of São Luís. São Luís, Brasil, 2016.

from an adaptation of the Self-Administered Physical Activity Checklist – SAPAC[17]. The physical activity index (AI) used was the sum of all activities carried out during the week [time of activity per day × MET (metabolic equivalent of the task) × number of days of activity per week]. This variable was categorized as: sedentary (AI = 0), low (1 ≤ AI < 600), moderate (600 ≤ AI < 3000), and high (AI ≥ 3000).

The maternal variables analyzed were maternal age (years, treated as a continuous numerical variable), pregestational BMI (kg/m², treated as a continuous numerical variable), smoking during pregnancy (answer to the question "Do you smoke?," which may have been no or yes), gestational weight gain (kg, treated as a continuous numerical variable), type of delivery (vaginal or cesarean) and gestational age (weeks, treated as a continuous numerical variable).

The variables for the newborn were sex (male or female) and birth length (cm, treated as a continuous numerical variable). The following variables were also used for the adolescents: "neither-nor" generation (studies and/or works and does not study nor work), and alcohol consumption (measured with the Alcohol Use Disorder Identification Test (AUDIT) and categorized as low, risky, harmful or probable dependence)[18].

The dependent variable was the quantity of FFM of the adolescents measured by DEXA and expressed as fat-free mass index (FFMI) (kg/m^2) and treated as a continuous numerical variable. This index is calculated by dividing adolescent FFM (kg) by height squared (m)[19].

Structural equation modeling was used to investigate the effect of the explanatory variables and covariables on the FFM of the adolescent. This modeling has the advantage of dealing simultaneously with multiple dependence relations and is able to represent non-observed concepts (latent variables) in these relations by modeling the error of measurement in the estimation process[20].

According to the theory proposed here, birth SES, maternal age, pregestational BMI, smoking during pregnancy, gestational weight gain, type of delivery, gestational age, sex of the newborn, birth length, BW, SES of the adolescent, "neither-nor" generation, level of physical activity, and alcohol consumption by the adolescent had a direct effect on the FFM of the adolescent.

Data were analyzed statistically using the Mplus software version 7. The Weighted Least Squares Mean and Variance Adjusted estimator (WLSWV) was used for the continuous and categorical variables. The THETA parameterization was used to control differences in residual variances. The following fit indices were considered in order to determine if the model showed good fit: a) p > 0.05 for the chi-square test (χ^2)[14]; b) value < 0.05 and an upper limit of the 90% confidence interval of less than 0.08 for the root mean square error of approximation (RMSEA)[15], and c) values of more than 0.95 for the Comparative Fit Index and the Tucker Lewis Index (CFI/TLI)[15].

In the analysis of the standardized estimates for the construction of the latent variables, a factor loading of more than 0.5 with p < 0.05 indicated a correlation of moderately high magnitude between the variables observed and the construct[14]. In order to obtain suggestions of changes in the initial hypotheses we estimated modification indices using the *modindices* command, whereby the proposed modifications considered to be plausible from a theoretical viewpoint and with a value of the modification index higher than 10 could be incorporated, generating a new model[15].

The total, direct and indirect effects of the latent and observed variables were evaluated in the final model. An effect was judged to be present when p < 0.05. The mean and standard deviation of the continuous variables was calculated in order to facilitate interpretation of the results. The result of the effect of the variable on the original metric was obtained by multiplying the value of the standardized coefficient of the total effect by the standard deviation of the variable (SC x SD).

To verify possible selection bias, the variables family income at birth and sex of the newborn were compared between those followed up and those lost to follow up. No formal sample size estimate was performed as it is not easily available in most used statistical programs, but we used as a rule of thumb a minimum of 20 observations per each variable included in the model. A sample size of 579 allowed us to include a maximum of 29 variables in the structural equation model, and we have included 17 variables.

This study complied with the formal requirements contained in the national and international standards of regulatory research involving human subjects.

RESULTS

Of the 579 adolescents studied, 59.4% were males, 77% reported studying or working, and 37.1% were sedentary. Mean pregestational BMI was 21.1 (SD = 2.8) kg/m^2 and BW was 3.2 (SD = 0.5) kg. Mean adolescent FFMI was 16 (SD = 2.4) kg/m^2. The remaining results are listed in Table 1.

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Table 1. Socioeconomic, demographic, family and adolescent characteristics of the RPS cohort of São Luís. São Luís, Brazil, 2016.

Variables	n	%
Sex of the newborn		
Male	344	59.4
Female	235	40.6
Head of family schooling at birth (years)		
Never studied	5	0.9
1 to 4	61	10.5
5 to 8	168	29.0
9 to 11	253	43.7
≥ 12	28	4.8
Unknown	64	11.1
Family income at birth (minimum wages)		
≤1	77	13.3
1.1 to 1,9	96	16.6
2 to 2.9	95	16.4
3 to 4,9	124	21.4
5 to 9,9	97	16.8
≥ 10	55	9.5
Unknown	35	6.0
Smoking during pregnancy		
No	549	94.8
Yes	30	5.2
Type of delivery		
Vaginal	355	61.3
Cesarean	224	38.7
Head of family schooling at adolescence (years))		
Never studied	11	1.9
1 to 4	139	24.0
5 to 8	288	49.7
9 to 11	19	3.3
≥ 12	60	10.4
Unknown	62	10.7
Family income at adolescence (minimum wages)		
≤ 1	114	19.7
1.1 to 1.9	128	22.1
2 to 2.9	118	20.4
3 to 4.9	87	15.0
5 to 9.9	52	9.0
≥ 10	20	3.4
Unknown	60	10.4
"Neither-nor generation"		
Studies or works	446	77.0
Does not study or work	133	23.0
Level of physical activity of the adolescent		
Sedentary	215	37.1
Low	81	14.0
Moderate	136	23.5
High	144	24.9
Unknown	3	0.5

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Table 1. Socioeconomic, demographic, family and adolescent characteristics of the RPS cohort of São Luís. São Luís, Brazil, 2016. Continue.

Alcohol consumption by the adolescent		
Low	471	81.4
Risky	90	15.5
Harmful	10	1.7
Probable dependence	8	1.4
Total	579	100.0
	Mean	**Standard deviation**
Maternal age (years)	23.4	5.3
Pregestational BMI (kg/m^2)	21.1	2.8
Gestational weight gain (kg)	9.7	5.0
Gestational age (weeks)	38.9	2.4
Birth weight (kg)	3.2	0.5
Birth length (cm)	48.9	2.4
Fat-free mass index of the adolescent (kg/m^2)	16.0	2.4

Table 2. Fit indices of the model for the fat-free mass outcome of the adolescents in the RPS cohort of São Luís. São Luís, Brazil, 2016.

Indices	Model[a]
χ^{2b}	
Value	137.594
Degrees of freedom	78
p-value	< 0.001
RMSEA[c]	
Value	0.036
90% confidence interval	0.026–0.046
p-value	0.990
CFI[d]	0.963
TLI[e]	0.936

[a] Initial and final model since there was no suggestion of plausible modification.
[b] Chi-square test.
[c] Root mean square error of approximation.
[d] Comparative Fit Index.
[e] Tucker Lewis Index.

The theoretical model showed good fit according to the RMSEA and CFI indicators, with no plausible suggestion of modification (Table 2). The latent variables SES at birth and at adolescence had all indicators showing factor loadings higher than 0.5 (p < 0.001) (Table 3).

The standardized coefficients of the direct effect of the indicator and latent variables on FFM of the adolescent are listed in Table 3. The total direct and indirect effects including their specific pathways are shown in Table 4.

Pregestational BMI had a positive total effect (Standardized Coefficient, SC = 0.152; p < 0.001) and direct effect (SC = 0.146; p < 0.001) on adolescent FFM. The increase of one standard deviation (SD) of pregestational BMI (2.8 kg/m^2) resulted in an FFM increase of 0.36 kg/m^2 during adolescence (Table 4).

Newborn's sex had negative total (SC = -0.633; p < 0.001) and direct (SC = -0.523; p < 0.001) effects, revealing that being a female implied a smaller FFM during adolescence. Newborn's sex also had a negative indirect effect (SC = -0.110; p < 0.001) on FFM, mainly in terms of physical activity of the adolescent (SC = -0.085; p < 0.001). A negative association was found between newborn's sex and level of physical activity (SC = -0.442; p < 0.001) (Tables 3 and 4).

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Table 3. Standardized coefficients, standard errors and p-values of the direct effects of the observed variables and constructs on fat-free mass of adolescents of the RPS cohort of São Luís. São Luís, Brazil, 2016.

Pathways and estimates	Standardized coefficient	Standard error	p-value
Latent variables			
SES at birth			
Head of family schooling at birth	0.713	0.040	< 0.001
Family income at birth	0.682	0.038	< 0.001
SES of the adolescent			
Head of family schooling during adolescence	0.649	0.050	< 0.001
Family income during adolescence	0.526	0.046	< 0.001
Direct effects			
Fat-free mass of the adolescent			
SES at birth	0.194	0.060	0.578
Maternal age	-0.130	0.040	0.001
Pregestational BMI	0.146	0.036	< 0.001
Smoking during pregnancy	0.048	0.058	0.403
Gestational weight gain	0.041	0.042	0.338
Type of delivery	0.081	0.056	0.151
Gestational age	-0.025	0.036	0.478
Sex of the newborn	-0.523	0.030	< 0.001
Birth length	-0.043	0.051	0.399
Birth weight	0.121	0.051	0.019
SES of the adolescent	-0.282	0.350	0.421
"Neither-nor" generation	-0.077	0.045	0.084
Level of physical activity of the adolescent	0.191	0.044	< 0.001
Alcohol consumption by the adolescent	0.054	0.052	0.300
Maternal age			
SES at birth	0.278	0.044	< 0.001
Pregestational BMI			
SES at birth	-0.088	0.055	0.109
Maternal age	0.299	0.043	< 0.001
Smoking during pregnancy			
SES at birth	-0.115	0.086	0.185
Gestational weight gain			
SES at birth	0.227	0.060	< 0.001
Maternal age	0.092	0.052	0.074
Pregestational BMI	-0.083	0.051	0.104
Smoking during pregnancy	0.067	0.124	0.591
Type of delivery			
SES at birth	0.452	0.057	< 0.001
Maternal age	0.175	0.049	< 0.001
Gestational weight gain	0.106	0.059	0.071
Gestational age			
Maternal age	-0.001	0.047	0.983
Gestational weight gain	0.127	0.044	0.004
Type of delivery	-0.091	0.059	0.123
Birth length			
SES at birth	-0.039	0.064	0.544

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Table 3. Standardized coefficients, standard errors and p-values of the direct effects of the observed variables and constructs on fat-free mass of adolescents of the RPS cohort of São Luís. São Luís, Brazil, 2016. Continuation.

Pregestational BMI	0.170	0.039	< 0.001
Gestational weight gain	0.117	0.043	0.007
Type of delivery	-0.098	0.068	0.146
Gestational age	0.374	0.028	< 0.001
Sex of the newborn	-0.037	0.043	0.386
Birth weight			
SES at birth	-0.030	0.047	0.521
Maternal age	0.091	0.039	0.020
Pregestational BMI	0.068	0.036	0.061
Smoking during pregnancy	-0.069	0.070	0.331
Gestational weight gain	0.090	0.034	0.008
Type of delivery	0.126	0.047	0.007
Gestational age	0.135	0.025	< 0.001
Sex of the newborn	0.014	0.030	0.644
Birth length	0.655	0.023	< 0.001
SES of the adolescent			
SES at birth	0.917	0.060	< 0.001
"Neither-nor" generation			
Sex of the newborn	0.158	0.055	0.004
SES of the adolescent	-0.073	0.070	0.303
Level of physical activity of the adolescent			
Sex of the newborn	-0.442	0.037	< 0.001
Birth weight	-0.072	0.046	0.122
SES of the adolescent	-0.057	0.053	0.283
"Neither-nor" generation	-0.114	0.058	0.048
Alcohol consumption by the adolescent			
Sex of the newborn	-0.038	0.067	0.570
SES of the adolescent	-0.001	0.072	0.994
"Neither-nor" generation	-0.103	0.082	0.207
Level of physical activity of the adolescent	0.293	0.070	< 0.001

SES: socioeconomic status; BMI: body mass index

Birth weight had a positive total (SC = 0.106; p = 0.034) and direct (SC = 0.121; p = 0.019) effect on FFM; for each 0.5 kg (1 SD) increase in BW there was a 0.25 kg/m² increase in FFMI during adolescence (Table 4).

The "neither-nor" generation variable had a negative total effect (SC = -0.106; p = 0.015) on FFM, although without significant direct or indirect effects. The rate of those neither studying nor working represented a reduction in FFM during adolescence (Table 4).

The level of physical activity of the adolescent had a positive total (SC = 0.207; p < 0.001) and direct (SC = 0.191; p < 0.001) effect, with a 0.5 kg/m² increase in FFM for each 1 SD increase in the level of physical activity (Table 4).

SES at birth and at adolescence had no total effect on adolescent FFM; similarly, the following variables also had no total effect: maternal age, smoking during pregnancy, gestational weight gain, type of delivery, BW, and alcohol consumption during adolescence (Table 4).

Losses to follow up were higher for the poor (78.5%) compared with the better off (73.4%, p = 0.013) and for females (79.8%) compared with males (73.4%, p < 0.001).

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Table 4. Standardized coefficients, standard errors and p-values of the total, direct and indirect effects of the observed variables and constructs on fat-free mass of adolescents of the RPS cohort of São Luís. São Luís, Brazil, 2016.

Pathways and estimates	Standardized coefficient	Standard error	p
Total, direct and indirect effects			
SES at birth			
Total	-0.050	0.045	0.266
Maternal age			
Total	-0.053	0.036	0.139
Pregestational BMI			
Total	0.152	0.035	< 0.001
Direct	0.146	0.036	< 0.001
Indirect	0.006	0.009	0.481
Smoking during pregnancy			
Total	0.045	0.057	0.429
Gestational weight gain			
Total	0.063	0.041	0.125
Type of delivery			
Total	0.092	0.054	0.091
Gestational age			
Total	-0.001	0.032	0.972
Sex of the newborn			
Total	-0.633	0.024	< 0.001
Direct	-0.523	0.030	< 0.001
Indirect	-0.110	0.020	< 0.001
Indirect specific			
Via level of physical activity of the adolescent	-0.085	0.021	< 0.001
Birth length			
Total	0.026	0.038	0.495
Birth weight			
Total	0.106	0.050	0.034
Direct	0.121	0.051	0.019
Indirect	-0.015	0.010	0.147
SES of the adolescent			
Total	-0.286	0.350	0.413
"Neither-nor" generation			
Total	-0.106	0.044	0.015
Direct	-0.077	0.045	0.084
Indirect	-0.029	0.015	0.050
Indirect specific			
Via level of physical activity of the adolescent	-0.022	0.012	0.075
Level of physical activity of the adolescent			
Total	0.207	0.040	< 0.001
Direct	0.191	0.044	< 0.001
Indirect	0.016	0.015	0.295
Alcohol consumption by the adolescent			
Total	0.054	0.052	0.300

SES: socioeconomic status; BMI: body mass index.

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DISCUSSION

In this study, higher values of pregestational BMI and BW and a higher level of physical activity resulted in increased FFM during adolescence. Being a female and not studying or working implied a smaller FFM during adolescence. Regarding the magnitude of the effects, the variables related to birth had a greater effect on adolescent FFM than the variables related to adolescence itself.

Pregestational BMI had a positive effect on FFM, a result also observed in a Brazilian cohort study in which a positive association was detected between pregestational maternal weight and FFMI, FM index and BMI of adolescents[21]. This finding might be explained by the fact that increases in maternal weight might be associated with proportional increases in FM and FFM of adolescents. A systematic review of 45 studies concluded that a high pregestational BMI increases the risk of high BW and later overweight/obesity in the offspring[22]. However, these studies used BMI as a method to assess nutritional status, so that it was not possible to evaluate in which body compartment an increase occurred[11].

A study conducted in Sweden assessed the body composition of 209 couples and their children by air displacement plethysmography and observed that the FFM of the parents was positively associated with the FFM of the newborn. The magnitude of the effect of parental FFM on newborn FFM was greater for mothers than for fathers, with the authors suggesting that the already known effect of maternal BMI on the BW of the infant was largely due to the effect of maternal FFM rather than FM[23]. Strong positive correlations have already been observed between FFM at birth and at four and six years of life[24], showing that this compartment can be preserved along life.

Birth weight had a positive effect on adolescent FFM. The association between higher BW and future overweight/obesity is well known[25], although a large part of the studies used BMI as an indicator of obesity. BMI is correlated with both FM and FFM; thus, the positive lifelong associations already detected between BW and BMI may show the effect of BW on FFM and not on FM[26].

Singhal et al.[26] observed that a higher BW was associated with a greater FFM among children and adolescents regardless of sex, age, pubertal status, physical activity, and height. A study published by a consortium which provided cohort data from five low and middle-income countries, including Brazil, also showed that BW was more associated with adult FFM than with FM[27].

The greatest negative effect detected in the analysis was that of females on FFM. There are specific differences in body composition between sexes: women have a relatively larger FM and men a larger FFM[28]. These differences are minimal during childhood but become more apparent during adolescence. At the end of this phase and during adulthood, men have on average 1.5 times more FFM than women[8].

The sex of the newborn also showed an indirect effect, being negative via physical activity level. Females were associated with a lower level of physical activity resulting in a smaller FFM during adolescence. A systematic review of 69 published studies show that, in Brazil, the highest prevalence of physical inactivity among adolescents was detected in females, with the magnitude of the difference between sexes ranging from 1% to 29.1%[29]. This discrepancy may involve self-efficacy, social support and motivation as factors differently impacting physical activity among women and men [30].

A higher level of physical activity resulted in higher FFM during adolescence. A prospective cohort was formed in Canada to investigate the independent effects of physical activity on FFM, considering the confounding effects of growth and biological maturation. The authors observed that habitual physical activity had an independent influence on the increase in FFM assessed by DEXA during adolescence in both sexes. In addition,

they observed that an equal increase in physical activity resulted in a 50% greater FFM accumulation for men than for women[8].

Not studying or working was associated with a smaller FFM during adolescence. The total effect was negative but there was no statistically significant direct or indirect effect, suggesting the sum of effects generated the total effect. Females were was positively associated with not studying or working, and adolescents included in this variable showed lower physical activity levels, a fact that may explain the negative effect of belonging to this group on FFM. There is evidence that spending a period of time not in employment, education or training (NEET) may have a harmful effect on the physical and mental health of young people, with this effect being stronger at younger ages or lasting longer during life[31].

A limitation of our study was the subjects lost to follow-up, especially during the third phase, due to the difficulty in locating the adolescents despite all the search strategies used. Losses to follow-up were higher among females and the poorest adolescents, which may have contributed to underestimating associations in which those strata had higher prevalence. With a larger sample, it may be possible to detect other effects of important determinants.

A strong point is the cohort type of the study, with its advantages regarding reverse causality and the possibility of follow-up of the same population. In addition, equipment considered to be the gold standard and quite accurate for the measurement of each body compartment was used for the evaluation of the body composition of the adolescents. Another relevant point is the statistical method used to analyze the effects of the determinants of FFM during adolescence, i.e., structural equation modeling. This method provides more comprehensive results by estimating various separate and interdependent multiple regression equations, allowing the estimate of total, direct and indirect effects between variables.

The main findings of this study show that the strongest determinant factors for FFM in adolescence are sex, level of physical activity of the adolescent, pregestational BMI, birth weight, and not studying nor working. Females have a greater effect on FFM than all other factors. These findings contribute to the advancement of knowledge in the area, mainly by using a reliable statistical method in a prospective cohort and support the importance of prenatal care of good quality and of a later encouragement of the practice of physical activity, especially among women since this group has a biological tendency to a smaller FFM in later phases of life.

REFERENCES

1. Moreira MEL, Goldani MZ. A criança é o pai do homem: novos desafios para a área de saúde da criança. Cienc Saude Coletiva. 2010;15(2):321-7. https://doi.org/10.1590/S141381232010000200002

2. Kuh D, Ben-Shlomo Y, editors. A life course approach chronic disease epidemiology. 2. ed. New York: Oxford University Press; 2004.

3. Orlandi SP, Schneider BC, Gonzalez MC, González-Chica DA, Assunção MCF. Determinantes nutricionais precoces da massa livre de gordura no início da vida adulta: revisão sistemática da literatura. Cad Saude Publica. 2013;29(4):639-53. https://doi.org/10.1590/S0102-311X2013000400003

4. Hitzl AP, Jörres RA, Heinemann F, Pfeifer M, Budweiser S. Nutritional status in patients with chronic respiratory failure receiving home mechanical ventilation: impact on survival. Clin Nutr. 2010;29(1):65-71. https://doi.org/10.1016/j.clnu.2009.08.002

5. Kimyagarov S, Klid R, Fleissig Y, Kopel B, Arad M, Adunsky A. Skeletal muscle mass abnormalities are associated with survival rates of institutionalized elderly nursing home residents. J Nutr Health Aging. 2012;16(5):432-6. https://doi.org/10.1007/s12603-012-0005-4

6. Soeters PB, Sobotka L. The pathophysiology underlying the obesity paradox. Nutrition. 2012;28(6):613-5. https://doi.org/10.1016/j.nut.2011.10.010

RSP

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7. Santanasto AJ, Goodpaster BH, Kritchevsky SB, Miljkovic I, Satterfield S, Schwartz AV, et al. Body composition remodeling and mortality: The Health Aging and Body Composition Study. J Gerontol A Biol Sci Med Sci. 2016;72(4):513-9. https://doi.org/10.1093/gerona/glw163

8. Baxter-Jones ADG, Eisenmann JC, Mirwald RL, Faulkner RA, Bailey DA. The influence of physical activity on lean mass accrual during adolescence: a longitudinal analysis. J Appl Physiol (1985). 2008;105(2):734-41. https://doi.org/10.1152/japplphysiol.00869.2007

9. Cheng S, Völgyi E, Tylavsky FA, Lyytikäinen A, Törmäkangas T, Xu L, et al. Trait-specific tracking and determinants of body composition: a 7-year follow-up study of pubertal growth in girls. BMC Med. 2009;7:5. https://doi.org/10.1186/1741-7015-7-5

10. Monyeki MA, Koppes LLJ, Monyeki KD, Kemper HCG, Twisk JWR. Longitudinal relationships between nutritional status, body composition, and physical fitness in rural children of South Africa: The Ellisras longitudinal study. Am J Hum Biol. 2007;19(4):551-8. https://doi.org/10.1002/ajhb.20616

11. Bann D, Wills A, Cooper R, Hardy R, Aihie Sayer A, Adams J, et al. Birth weight and growth from infancy to late adolescence in relation to fat and lean mass in early old age: findings from the MRC National Survey of Health and Development. Int J Obes (Lond). 2014;38(1):69-75. https://doi.org/10.1038/ijo.2013.115

12. Ylihärsilä H, Kajantie E, Osmond C, Forsén T, Barker DJ, Eriksson JG. Body mass index during childhood and adult body composition in men and women aged 56-70 y. Am J Clin Nutr. 2008;87(6):1769-75. https://doi.org/10.1093/ajcn/87.6.1769

13. Santos S, Severo M, Gaillard R, Santos AC, Barros H, Oliveira A. The role of prenatal exposures on body fat patterns at 7 years: intrauterine programming or birthweight effects? Nutr Metab Cardiovasc Dis. 2016;26(11):1004-10. https://doi.org/10.1016/j.numecd.2016.06.010

14. Kline RB. Principles and practice of structural equation modeling. 4. ed. New York: The Guilford Press; 2015.

15. Wang J, Wang X. Structural equation modeling: applications using Mplus. New York: John Wiley & Sons; 2012. (Wiley Series in Probability and Statistics).

16. Silva AAM, Coimbra LC, Silva RA, Alves MTSSB, Lamy Filho F, Lamy ZC, et al. Perinatal health and mother-child health care in the municipality of São Luís, Maranhão State, Brazil. Cad Saude Publica. 2001;17(6):1412-23. https://doi.org/10.1590/S0102-311X2001000600012

17. Sallis JF, Strikmiller PK, Harsha DW, Feldman HA, Ehlinger S, Stone EJ, et al. Validation of interviewer-and self-administered physical activity checklists for fifth grade students. Med Sci Sports Exerc. 1996;28(7):840-51. https://doi.org/10.1097/00005768-199607000-00011

18. Moretti-Pires RO, Corradi-Webster CM. Adaptação e validação do Alcohol Use Disorder Identification Test (AUDIT) para população ribeirinha do interior da Amazônia, Brasil. Cad Saude Publica. 2011;27(3):497-509. https://doi.org/10.1590/S0102-311X2011000300010

19. VanItallie TB, Yang MU, Heymsfield SB, Funk RC, Boileau RA. Height-normalized indices of the body's fat-free mass and fat mass: potentially useful indicators of nutritional status. Am J Clin Nutr. 1990;52(6):953-9. https://doi.org/10.1093/ajcn/52.6.953

20. Hair JF Jr, Black WC, Babin BJ, Anderson RE, Tatham RL. Análise multivariada de dados. Porto Alegre, RS: Bookman Editora; 2009.

21. Gigante DP, Victora CG, Horta BL, Lima RC. Undernutrition in early life and body composition of adolescent males from a birth cohort study. Br J Nutr. 2007;97(5):949-54. https://doi.org/10.1017/S0007114507433025

22. Yu Z, Han S, Zhu J, Sun X, Ji C, Guo X. Pre-pregnancy body mass index in relation to infant birth weight and offspring overweight/obesity: a systematic review and meta-analysis. PLoS One. 2013;8(4):e61627. https://doi.org/10.1371/journal.pone.0061627

23. Henriksson P, Löf M, Forsum E. Parental fat-free mass is related to the fat-free mass of infants and maternal fat mass is related to the fat mass of infant girls. Acta Paediatr. 2015;104(5):491-7. https://doi.org/10.1111/apa.12939

24. Crozier SR, Inskip HM, Godfrey KM, Cooper C, Harvey NC, Cole ZA, et al. Weight gain in pregnancy and childhood body composition: findings from the Southampton Women's Survey. Am J Clin Nutr. 2010;91(6):1745-51. https://doi.org/10.3945/ajcn.2009.29128

25. Dietz WH. Critical periods in childhood for the development of obesity. Am J Clin Nutr. 1994;59(5):955-9. https://doi.org/10.1093/ajcn/59.5.955

RSP

Determinants of fat-free mass in adolescents   Lima RJCP et al.

26. Singhal A, Wells J, Cole TJ, Fewtrell M, Lucas A. Programming of lean body mass: a link between birth weight, obesity, and cardiovascular disease? Am J Clin Nutr. 2003;77(3):726-30. https://doi.org/10.1093/ajcn/77.3.726

27. Kuzawa CW, Hallal PC, Adair L, Bhargava SK, Fall CHD, Lee N, et al. Birth weight, postnatal weight gain and adult body composition in five low and middle income countries. Am J Hum Biol. 2012;24(1):5-13. https://doi.org/10.1002/ajhb.21227

28. Schorr M, Dichtel LE, Gerweck AV, Valera RD, Torriani M, Miller KK, et al. Sex differences in body composition and association with cardiometabolic risk. Biol Sex Differ.2018;9(1):28. https://doi.org/10.1186/s13293-018-0189-3

29. Barbosa Filho VC, Campos W, Lopes AS. Epidemiology of physical inactivity, sedentary behaviors, and unhealthy eating habits among Brazilian adolescents: a systematic review. Cienc Saude Coletiva. 2014;19(1):173-94. https://doi.org/10.1590/1413-81232014191.0446

30. Edwards ES, Sackett SC. Psychosocial variables related to why women are less active than men and related health implications. Clin Med Insights Womens Health. 2016;9 Suppl 1:47-56. https://doi.org/10.4137/CMWH.S34668

31. Public Health England; Institute of Health Equity. Local action on health inequalities: reducing the number of young people not in employment, education or training (NEET). London (UK): PHE, IHE;2014. (Healthy Equity Evidence Review, 3).