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Growth patterns in early childhood and the onset of menarche before age twelve

Padrões de crescimento na infância precoce e ocorrência de menarca antes de doze anos de idade

ABSTRACT

OBJECTIVE: To examine the relationship between growth patterns in early childhood and the onset of menarche before age 12.

METHODS: The study included 2,083 women from a birth cohort study conducted in the city of Pelotas, Southern Brazil, starting in 1982. Anthropometric, behavioral, and pregnancy-related variables were collected through home interviews. Statistical analyses were performed using Pearson's chi-square and chi-square test for linear trends. A multivariable analysis was carried out using Poisson regression based on a hierarchical model.

RESULTS: Mean age of menarche was 12.4 years old and the prevalence of menarche before age 12 was 24.3%. Higher weight-for-age, height-for-age, and weight-for-height z-scores at 19.4 and 43.1 months of age were associated with linear tendencies of increased prevalence and relative risks of the onset of menarche before age 12. Girls who experienced rapid growth in weight-for-age z-score from birth to 19.4 months of age and in weight-for-age or height-for-age z-scores from 19.4 to 43.1 months of age also showed higher risk of menarche before age 12. Higher risk was seen when rapid growth in weight-for-age z-score was seen during these age intervals and the highest risk was found among those in the first tertile of Williams' curve at birth. Rapid growth in weight-for-height z-score was not associated with menarche before age 12.

CONCLUSIONS: Menarche is affected by nutritional status and growth patterns during early childhood. Preventing overweight and obesity during early childhood and keeping a "normal" growth pattern seem crucial for the prevention of health conditions during adulthood.

DESCRIPTORS: Menarche. Puberty. Child Development. Adolescent Development. Sexual Maturation. Body Weights and Measures. Risk Factors. Cohort Studies. Weight by age. Height by Weight. Height by Age.

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RESUMO

OBJETIVO: Avaliar a relação entre padrões de crescimento na infância precoce e ocorrência de menarca antes de 12 anos de idade.

MÉTODOS: O estudo incluiu 2.083 mulheres do estudo de coorte de nascidos em Pelotas, RS, de 1982. Variáveis antropométricas, comportamentais e relacionadas à gestação foram coletadas por meio de entrevistas domiciliares. As análises estatísticas empregadas foram o qui-quadrado de Pearson e qui-quadrado para tendência linear. Além disso, análise multivariável foi realizada usando a regressão de Poisson, seguindo um modelo hierárquico.

RESULTADOS: A média de idade da menarca foi de 12,4 anos e a prevalência de menarca antes dos 12 anos foi de 24,3%. Maiores valores de escores Z nos índices peso/idade, altura/idade e peso/altura aos 19,4 e 43,1 meses corresponderam a maiores riscos de apresentar menarca antes dos 12 anos. Esse risco foi sistematicamente maior na idade de 43,1 meses. Meninas que experimentaram rápido crescimento em escore Z de peso/idade entre o nascimento e 19,4 meses ou em escore Z de peso/idade ou altura/idade entre 19,4 e 43,1 meses, mostraram os maiores riscos. O risco de menarca antes dos 12 anos foi mais elevado quando o crescimento rápido em escore Z de peso/idade ocorreu em ambos os períodos; e ainda maior entre as meninas do primeiro tercil da curva de Williams. Crescimento rápido em escore Z de peso/altura não esteve associado com menarca antes dos 12 anos.

CONCLUSÕES: A idade da menarca mostrou-se influenciada pelo estado nutricional e padrões de crescimento durante a infância precoce. Assim, evitar sobrepeso e obesidade na infância precoce mantendo um padrão "normal" de crescimento parece ser importante para prevenir problemas de saúde em futuras etapas da vida.

DESCRITORES: Menarca. Puberdade. Desenvolvimento Infantil. Desenvolvimento do Adolescente. Maturidade Sexual. Pesos e Medidas Corporais. Fatores de Risco. Estudos de Coortes. Peso para Idade. Peso para Altura. Altura para Idade.

INTRODUCTION

Menarche (first menstrual bleeding) is a milestone in female reproductive life and has been reported as an important predictor of health status during adolescence, adulthood, and post-menopause. Early menarche has been described as a risk factor for chronic diseases, especially breast cancer.[5]

The 1982 Pelotas Birth Cohort Study found high body mass index (BMI) and lower increment in weight gain after adolescent pregnancy among girls who experienced menarche before age 12,[13] and lower stature at 19 when menarche was before 13.[14]

Studies suggest chronic diseases are programmed by restrictive environments during intrauterine life resulting in abnormally programmed metabolic pathways that act regulating metabolic, hormonal adaptive capacities in future life.[2,12] Therefore, identifying early health determinants and adopting the so-called life course approach[6,18] are new goals of epidemiology and public health.[20] Early childhood has been also described as a "window" for programming of chronic disease and there is evidence that rapid growth can produce negative health effects in later life.[7-9,11,17,19,21,22] If rapid growth occurs after a "restriction" period, known as catch-up growth, it could have short-term benefits with lower rates of infections during childhood.[23] However, weight gain in the first two years of life has been associated with lean mass in 18-year-old males in Brazil, whereas later weight gain was more strongly associated with fat mass.[26]

There are scarce studies investigating the association between early events and early menarche. Some authors have identified an association between the timing of puberty and early weight gain,[1,7] but no association was found with low birthweight.[1] Other studies reported an association between low birthweight and early puberty.[7,16]

The objective of the present study was to examine the relationship between growth patterns during early childhood and the onset of menarche before age 12.

METHODS

The 1982 Pelotas Birth Cohort Study included 5,914 live born births. The cohort subjects have been followed up in several studies and detailed information are available elsewhere.[24,25] The present study included 2,084 women with information on menarche. One subject was excluded due to a uterine tumor; thus the final sample comprised 2,083 women.

The study was based on information from the perinatal study (1982) and follow-up studies in 1984, 1986 and 2004–2005. In summary, in 1982, all subjects were weighed and their mothers answered a questionnaire on socioeconomic, demographic and health-related conditions. Data on their length at birth was not collected. During the 1984 and 1986 follow-up studies, the mothers or caretakers answered a questionnaire and their children had weight and height measurements taken. Subjects were on average 19.4 and 43.1 months old and 12.8% and 15.9% from the original cohort were lost to follow-up, respectively. Likewise, in 2004–2005, subjects were 23–24 years old and 22.6% from the original cohort were lost to follow-up. Interviewers were thoroughly trained before fieldwork and quality control included repeating 5% of the interviews and double data entry.

Confounders in the perinatal study included skin color, family income (in quintiles of minimum monthly wages), smoking during pregnancy and pre-gestational maternal BMI. Weight-for-age z-scores using Williams' curve[27] were used to generate other variables. In addition, from the 1984 and 1986 follow-up studies, breastfeeding duration was used for control of confounding. Height, weight and age were used to generate weight-for-age, height-for-age and weight-for-height z-scores based on the 2006 World Health Organization (WHO) curves,[4] and were categorized as ≤0, 0.01 to 1, 1.01 to 2, and >2.

Growth patterns were analyzed at two age intervals (interval 1 and 2): from birth to 19.4 months of age; and from 19.4 to 43.1 months of age. For interval 1, the change in weight-for-age z-score was a result of "z-score at 19.4 months of age *minus* z-score using Williams' curve". For interval 2, it was a result of "z-score at 43.1 months of age *minus* z-score at 19.4 months of age".

The change in height-for-age and weight-for-height z-scores was analyzed separately in interval 2 as "z-score at 43.1 months of age *minus* z-score at 19.4 months of age," respectively. Rapid growth has been described as gain of more than 0.67 z-score,[21] used as a cut-off in other studies.[19,23] In addition, z-scores were defined as "catch-down growth" if they were ≤–0.67; "normal" if between –0.669 and 0.669; and "rapid growth" if ≥0.67. Otherwise, a variable analyzing change in both intervals in weight-for-age z-score was generated as "never rapid growth" (if catch-down or normal growth in intervals 1 and 2); "rapid growth/no rapid growth"; "no rapid growth/rapid growth" (if normal or catch-down growth in interval 1 and rapid growth in interval 2); and "always rapid growth" (rapid growth in both intervals 1 and 2). These analyses were performed in the entire sample and stratified by tertiles of z-scores at the beginning of each age interval (at birth and 19.4 months of age).

The age of menarche was obtained from the 2004–2005 follow-up and was analyzed as a dichotomous outcome: <12 and ≥12 years old.

Pearson's chi-square and chi-square test for linear trends were used. A multivariable analysis was performed using Poisson regression with a robust variance estimative to obtain prevalence ratios.[3] The regression was based on a hierarchical model (Figure).

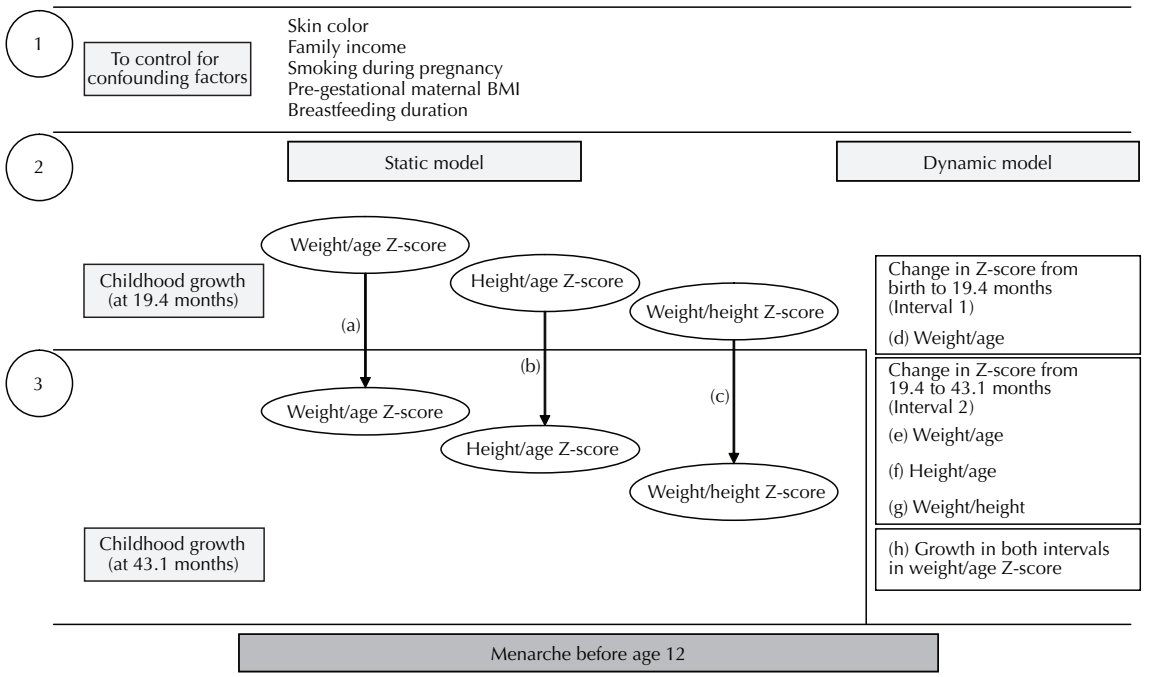
All potential confounders (Figure) were cross-tabulated against the outcome and explanatory variables and only those showing an association ($p<0.20$) were included in the multivariable analysis. Confounding was defined as the difference between crude and adjusted estimates higher than 10%.

In levels 2 and 3 (Figure), two independent models – one "static" and the other "dynamic" – were analyzed and designated by letters (a through g). The variables in the level 3 were adjusted for the related "static" model in the level 2 (letters a–c) and for variables in the level 1, but not between them. The variables in the level 2 included in the "dynamic" model (letters d–g) were adjusted only for the level 1, but not between them.

Using the actual sample size, prevalence ratio was estimated with a power of 80% and at 5% significance level. Some independent variables showed missing data: change in weight-for-age z-score in interval 1 (26.1%) and change in weight-for-age z-score in both intervals (30.7%). Moreover, the characteristics of subjects with missing data had a similar distribution for family income quintiles, indicating that they were not different from the study subjects. The number of observations for each regression model is included in the respective tables.

The analyses were performed using Stata 9.

All followed-up subjects signed an informed consent. The study was approved by the Research Ethics Committee of *Universidade Federal de Pelotas*.



Superior levels determine inferior levels. The numbers represent the levels from distal to proximal determination of causality. In level 2, independent models are denoted by letters (a) through (h). The variables in level 3 were adjusted for the corresponding static model in level 2 (letters a-c) and the other exposures from level 1, and never among themselves. Those variables from level 2 that reflect change in anthropometric characteristics (letters d-h; dynamic model) were adjusted only for level 1 and never among themselves.

Figure. Hierarquical model approach for the onset of menarche before age 12.

RESULTS

Mean age of menarche was 12.44 years old (95% CI: 12.38; 12.51); median age was 12 years old and the standard error was 1.51. The prevalence of menarche before 12 was 24.3% (95% CI: 22.5; 26.2) and 66.8% and 8.9% between age 12 and 14 and older than 14, respectively. In addition, the asymmetry coefficient was equal to 0.15 with Kurtosis of 3.53, indicating near-normal frequency distribution.

Table 1 shows a summary description of the sample including skin color, family income, smoking during pregnancy, anthropometric and growth pattern variables, among others. There were a higher proportion of girls who experienced rapid growth with change in weight-for-age z-score from birth to 19.4 months of age (41.0%) than from 19.4 to 43.2 months of age (8.0%).

The differences in proportions of menarche before age 12 and Poisson regression results by z-score groups are showed in Table 2. Increasing weight-for-age, height-for-age and weight-for-height z-scores at 19.4 and 43.1 months of age were associated to linear tendencies of increasing prevalence of the outcome. The prevalence and relative risks of menarche before age 12 were systematically higher in those with z-scores >2 or more at 43.1 months than at 19.4 months of age. On the other hand, weight-for-age z-score >2 at 19.4 and 43.1 months of age showed higher risk of the outcome compared to ≤0 z-score group. Negative confounding was detected at 43.1 months of age (crude PR=2.13; p<0.001; adjusted PR=2.66; p<0.001).

Height-for-age z-score (Table 2) at 19.4 months and 43.1 months old showed that taller girls were more likely to have menarche before 12 than shorter ones (p<0.001). The association at 43.1 months of age had a negative confounding effect (crude PR=2.26; p<0.001; adjusted PR=2.97; p<0.001). The analysis of weight-for-height z-score revealed that the >2 group at 43.1 months of age had the highest risk of the outcome and had a positive confounding effect (crude PR=1.95; p<0.001; adjusted PR=1.73; p=0.002).

Table 3 shows the results for growth variables. In interval 1, girls who experienced rapid growth in weight-for-age z-score showed the highest prevalence of the outcome (29.2%; p<0.001). The same was seen in interval 2, but with greater prevalence of menarche before age 12 (34.3%; p<0.001) than in interval 1. In fact, those who experienced rapid growth in both intervals had the highest prevalence of the outcome (37.8%; p<0.001) while those who experienced rapid growth in height-for-age z-score during interval 2 had the

Table 1. Characteristics of the sample (N=2,083). City of Pelotas, Southern Brazil, 2004-2005.

Variable	n	%
Skin color[a]	2080	
White	1713	82.4
Non-white	367	17.6
Family income (quintiles of minimum monthly wages)	2083	
1st	384	18.4
2nd	437	21.0
3rd	436	20.9
4th	412	19.8
5th	414	19.9
Smoking during pregnancy[a]	2078	
No	1341	64.5
Yes	737	35.5
Pre-gestational maternal BMI (kg/m^2)[a]	1748	
<18	64	3.6
18 to 25	1272	72.8
>25 to 30	328	18.8
>30	84	4.8
Breastfeeding duration (months)[a]	2027	
≤1	417	20.6
1.1 to 3	528	26.1
3.1 to 6	469	23.1
>6	613	30.2
Weight-for-height z-score at 19.4 months[a]	1924	
≤ 0	490	25.5
0.01 to 1	829	43.1
1.01 to 2	486	25.3
> 2	119	6.2
Weight-for-height z-score at 43.1 months[a]	1888	
≤0	550	29.1
0.01 to 1	815	43.2
1.01 to 2	410	21.7
> 2	113	6.0
Weight-for-age z-score at 19.4 months[a]	1925	
≤ 0	832	43.2
0.01 to 1	729	37.9
1.01 to 2	302	15.7
> 2	62	3.2
Weight-for-age z-score at 43.1 months[a]	1889	
≤0	1000	52.9
0.01 to 1	622	32.9
1.01 to 2	209	11.1
>2	58	3.1
Height-for-age z-score at 19.4 months[a]	1926	
≤0	1358	70.5
0.01 to 1	423	22.0
1.01 to 2	121	6.2
>2	24	1.3

To be continued

Table 1 continuation

Variable	N	%
Height-for-age z-score at 43.1 months[a]	1889	
≤0	1390	73.6
0.01 to 1	382	20.2
1.01 to 2	96	5.1
>2	21	1.1
Change in weight-for-age z-score from birth to 19.4 months[b] (Interval 1)	1540	
Catch-down growth	243	15.8
Normal growth	666	43.2
Rapid growth	631	41.0
Change in weight-for-age z-score from 19.4 to 43.1 months[a] (Interval 2)	1796	
Catch-down growth	349	19.4
Normal growth	1304	72.6
Rapid growth	143	8.0
Change in weight-for-age z-score in both intervals[b]	1443	
Never rapid growth	777	53.9
Rapid growth/no rapid growth	556	38.5
No rapid growth/rapid growth	65	4.5
Always rapid growth	45	3.1
Change in weight-for-height z-score from 19.4 to 43.1 months[a] (Interval 2)	1794	
Catch-down growth	327	18.2
Normal growth	1209	67.4
Rapid growth	258	14.4
Change in height-for-age z-score from 19.4 to 43.1 months old[a] (Interval 2)	1797	
Catch-down growth	15.14	15.1
Normal growth	73.62	73.6
Rapid growth	11.24	11.3

[a] Missing data lower than 16%
[b] Missing data between 20% and 30.7%
BMI: Body mass index

highest prevalence of the outcome (34.2%; p<0.001). Moreover, a change in weight-for-height z-score was not associated with the outcome (p=0.22).

In contrast, in interval 1 (Table 3), those girls who experienced rapid growth in weight-for-age z-score had higher risk than those who experienced catch-down growth in both crude (PR=1.65; p<0.001) and adjusted analyses (PR=1.75; p<0.001). The same was found in interval 2 with a relative risk very similar to that seen in interval 1 (crude PR=1.68; p=0.003; adjusted PR=1.82; p=0.002). Girls who experienced rapid growth in both intervals had the highest risk for the outcome (crude PR=1.79; p<0.001; adjusted PR=2.01; p<0.001) and those who experienced rapid growth in height-for-age z-score during interval 2 showed the highest relative risk for the outcome (crude PR1.79; p<0.001; adjust PR 1.96; p<0.001). Change in weight-for-height z-score was not associated with the outcome in crude analyses (p=0.2) but was marginally associated after controlling for confounders (PR=1.28; p=0.07).

Table 4 shows the relative risks of menarche before age 12 by growth patterns, taking into account the subjects' initial z-score tertiles adjusted by family income. This analysis was not adjusted for all confounders due to missing data that resulted in a lower number of subjects in each stratum: the program analyzes only those observations that include information for all variables of the model, which reduces the number of observations studied. To avoid the loss of many observations, the model was only adjusted for family income. In addition, family income was the only variable with no missing data. Girls in the first tertile of Williams' curve who experienced rapid growth in interval 1 showed the highest risk of the outcome (crude PR=2.10; p=0.01; adjusted PR=2.09; p=0.01). Those in the second or third tertiles had lower risk. When rapid growth occurred in

Table 2. Frequency distributions of menarche before age 12 by z-score groups. Crude and adjusted Poisson regression analyses by hierarchical approach. City of Pelotas, Southern Brazil, 2004-2005.

Level	Variable	n	Prevalence (95% CI)	p-value	Crude PR (95% CI)	p-value	Adjusted[a] PR (95% CI)	p-value	n[b]
2	Weight-for-age z-score at 19.4 months	1925		<0.001[c]		<0.001[d]		0.001[d]	1610
	≤ 0	832	19.2 (16.5;21.9)		1		1		
	0.01 to 1	729	27.6 (24.3;30.8)		1.43 (1.19;1.72)		1.43 (1.16;1.77)		
	1.01 to 2	302	29.8 (24.6;35.0)		1.55 (1.24;1.93)		1.54 (1.20;1.98)		
	>2	62	32.3 (20.3;44.2)		1.68 (1.14;2.47)		1.53 (0.97;2.37)		
3	Weight-for-age z-score at 43.1 months	1889		<0.001[c]		<0.001[d]		<0.001[d]	1503
	≤0	1000	17.8 (15.4;20.2)		1		1[e]		
	0.01 to 1	622	28.5 (24.9;32.0)		1.60 (1.33;1.92)		1.56 (1.22;1.98)		
	1.01 to 2	209	35.9 (29.3;42.4)		2.02 (1.61;2.52)		2.14 (1.56;2.95)		
	>2	58	37.9 (25.1;50.8)		2.13 (1.49;3.04)		2.66 (1.66;4.26)		
2	Height-for-age z-score at 19.4 months	1926		0.003[c]		0.002[d]		0.01[d]	1611
	≤0	1358	22.5 (20.3;24.7)		1		1		
	0.01 to 1	423	28.1 (23.8;32.4)		1.25 (1.04;1.50)		1.24 (1.02;1.52)		
	1.01 to 2	121	30.6 (22.2;38.9)		1.36 (1.02;1.81)		1.35 (0.98;1.86)		
	>2	24	33.3 (12.3;53.7)		1.48 (0.83;2.63)		1.48 (0.77;2.84)		
3	Height-for-age z-score at 43.1 months			<0.001[c]		<0.001[d]		<0.001[d]	1504
	≤0	1390	21.1 (18.9;23.2)		1		1[e]		
	0.01 to 1	382	30.1 (25.5;34.7)		1.43 (1.19;1.72)		1.54 (1.19;1.99)		
	1.01 to 2	96	36.5 (26.6;46.3)		1.73 (1.30;2.29)		2.39 (1.62;5.42)		
	>2	21	47.6 (24.3;70.9)		2.26 (1.42;3.58)		2.97 (1.58;6.32)		
2	Weight-for-height z-score at 19.4 months			<0.001[c]		<0.001[d]		0.003[d]	1609
	≤0	490	18.8 (15.3;22.2)		1		1		
	0.01 to 1	829	24.5 (21.5;27.4)		1.30 (1.05;1.62)		1.39 (1.09;1.78)		
	1.01 to 2	486	28.8 (24.8;32.8)		1.53 (1.22;1.93)		1.53 (1.18;1.99)		
	>2	119	29.4 (21.1;37.7)		1.57 (1.12;2.19)		1.49 (0.99;2.07)		

To be continued

Table 2 continuation

Level	Variable	n	Prevalence (95% CI)	p-value	Crude PR (95% CI)	p-value	Adjusted[a] PR (95% CI)	p-value	n[b]
3	Weight-for-height z-score at 43.1 months			<0.001[c]		<0.001[d]		0.002[d]	1501
	≤0	550	18.2 (14.9;21.4)		1		1[e]		
	0.01 to 1	815	22.8 (19.9;25.7)		1.25 (1.01;1.56)		1.20 (0.92;1.57)		
	1.01 to 2	410	30.7 (26.2;35.2)		1.69 (1.34;2.12)		1.52 (1.11;2.08)		
	>2	113	35.4 (26.4;44.3)		1.95 (1.43;2.64)		1.73 (1.15;2.59)		

[a] Adjusted for skin color, family income, smoking during pregnancy, pre-gestational maternal BMI, breastfeeding duration
[b] Observations in the regression model
[c] χ^2 test for linear trend
[d] Wald test for linear trend
[e] Also adjusted for the homologous z-score at 19.1 months

interval 2, the girls in the first and second tertiles had no risk (p=0.2). Those girls in the third tertile showed higher relative risks than those who experienced catch-down growth (crude PR=1.92; p=0.02; adjusted PR=1.98; p=0.02). Otherwise, when there was rapid growth in both intervals, girls in the first tertile showed the highest risk (crude PR=2.87; p=0.01; adjusted PR=2.85; p=0.01).

Changes in weight-for-age z-score in interval 2 (Table 4) were analyzed taking account weight-for-age z-score tertiles at 19.4 months of age. The risk increased among girls in the highest tertiles (crude PR=2.14; p=0.001; adjusted PR=2.14; p<0.001). Changes in height-for-age z-score in interval 2 showed that the relative risk for the outcome was similar in height-for-age z-score tertiles at 19.4 months of age and higher among those who experienced rapid growth. Finally, changes in weight-for-height z-score in interval 2 showed increased risk only in the third tertile (PR=1.83, p=0.001).

DISCUSSION

The study findings are consistent with Dunger et al[8] reports that place great importance on rapid growth during childhood associated with the onset of puberty. In our study (dynamic model), girls who experienced rapid growth and weight gain during an early age interval showed less apparent risk for menarche before age 12 than those who experienced rapid growth in a later period. After stratifying by tertiles of Williams' curve, the risk of the outcome was clearly higher among "small" girls at birth who experienced rapid growth in both age intervals. Moreover, the first interval studied seems to have a more remarkable negative effect on these girls. This early accelerated weight gain was associated with younger age of menarche, corroborating other studies.[1,8]

There is biological plausibility in our findings regarding the association of early rapid growth and menarche before age 12. A study analyzing a sub-sample of subjects from the 1982 Pelotas Birth Cohort from same age intervals showed an association between rapid growth and overweight/obesity in adolescence.[19] This finding could in part explain the mechanism that associates catch-up or rapid growth with age of menarche. These girls tend to have more body fat and it is well-recognized that greater body fat increases the risk for early menarche,[8] possibly due to high levels of leptin.[1,8]

There could be other explanations for the effect of rapid growth on the onset of menarche before age 12 rather than obesity. High leptin levels following rapid weight gain during childhood may trigger early pubertal development.[8]

The present study found that higher weight-for-age and/or height-for-age z-scores during early childhood (static model) was associated with menarche before age 12, which is consistent to that described in other studies.[1,7, 8,16]

The analysis of nutritional status (static model) separately from growth patterns (dynamic model) could be a useful yet challenging approach in life course epidemiology.[6,18] We believe that both models analyze the same issue but from different perspectives. The dynamic model had the advantage of describing the relative risk, especially in girls who were "small" at birth (first tertile of Williams' curve). For example, a risk was seen among girls who grew ≥0.67 z-score but did not reach the classic >2 z-score (static model) at 19.4 or at 43.1 months of age. However, further studies are required to estimate specificity and sensibility of each approach. Both models allow the assessment of relative risks of developing health conditions in future life at the individual level.

Table 3. Frequency distribution of menarche before age 12 by growth patterns considering z-score change during childhood. Crude and adjusted Poisson regression analyses by hierarchical approach. City of Pelotas, Southern Brazil, 2004-2005.

Variable	n	Prevalence (95% CI)	p-value	Crude PR (95% CI)	p-value	Adjusted[a] PR (95% CI)	p-value	n[b]
Change in weight-for-age z-score								
Interval 1[c]	1540		<0.001[d]		<0.001[e]		0.001[e]	1348
Catch-down growth	243	17.7 (12.9;22.5)		1		1		
Normal growth	666	21.6 (18.5;24.8)		1.22 (0.90;1.66)		1.27 (0.91;1.78)		
Rapid growth	631	29.2 (25.6;32.7)		1.65 (1.22;2.22)		1.75 (1.27;2.43)		
Interval 2[f]	1796		0.002[d]		0.003[e]		0.002[e]	1503
Catch-down growth	348	20.3 (16.1;24.6)		1		1		
Normal growth	1308	24.4 (22.0;26.7)		1.20 (0.95;1.51)		1.22 (0.96;1.56)		
Rapid growth	140	34.3 (26.4;42.1)		1.68 (1.24;2.29)		1.82 (1.31;2.54)		
Growth in both intervals	1443		<0.001[g]		<0.001[h]		<0.001[h]	1262
Never rapid growth	777	19.3 (16.5;22.1)		1		1		
Rapid/no rapid	556	28.2 (24.5;32.0)		1.46 (1.20;1.78)		1.50 (1.15;1.82)		
No rapid/rapid	65	30.8 (19.2;42.3)		1.59 (1.08;2.36)		1.73 (1.21;2.88)		
Always rapid growth	45	37.8 (23.0;52.5)		1.96 (1.31;2.92)		2.01 (1.35;3.14)		
Change in height-for-age z-score								
Interval 2[f]	1797		<0.001[d]		<0.001[e]		<0.001[e]	1504
Catch-down growth	272	19.1 (14.4;23.8)		1		1		
Normal growth	1323	23.3 (21.7;26.3)		1.25 (0.96;1.63)		1.38 (1.03;1.86)		
Rapid growth	202	34.2 (27.6;40.7)		1.79 (1.31;2.44)		1.96 (1.39;2.78)		
Change in weight-for-height z-score								
Interval 2[f]	1794		0.2[g]		0.2[h]		0.07[h]	1501
Catch-down growth	327	23.8 (19.2;28.5)		1		1		
Normal growth	1209	23.6 (21.2;27.0)		0.99 (0.79;1.23)		0.97 (0.77;1.24)		
Rapid growth	258	28.7 (23.1;34.2)		1.20 (0.92;1.58)		1.28 (0.95;1.72)		

[a] Adjusted for family income, skin color, smoking during pregnancy, pre-gestational maternal BMI and breastfeeding duration
[b] Observations into regression model
[c] From birth to 19.4 months
[d] χ^2 test for linear trend
[e] Wald test for trend
[f] From 19.4 to 43.1 months
[g] χ^2 test
[h] Wald test

Table 4. Prevalence ratio for menarche before age 12 according to growth patterns. Crude and adjusted analyses stratified by z-score tertile at the beginning of each age interval studied. City of Pelotas, Southern Brazil, 2004-2005.

Variable	First tertile		Second tertile		Third tertile	
	Crude PR (95% CI)	Adjusted[a] PR (95% CI)	Crude PR (95% CI)	Adjusted[a] PR (95% CI)	Crude PR (95% CI)	Adjusted[a] PR (95% CI)
	Weight-for-age z-score using Williams' curves					
Change in weight-for-age z-score in Interval 1						
	n=491 p=0.01[b]	n=491 p=0.01[b]	n=549 p=0.02[b]	n=549 p=0.02 [b]	n=500 p=0.02[b]	n=500 p=0.01[b]
Catch-down growth	1	1	1	1	1	1
Normal growth	1.33 (0.54;3.23)	1.34 (0.54;3.27)	1.32 (0.69;2.49)	1.34 (0.70;2.56)	1.22 (0.82;1.82)	1.24 (0.83;1.86)
Rapid growth	2.10 (0.91;4.85)	2.09 (0.90;4.88)	1.75 (0.93;3.28)	1.79 (0.94;3.40)	1.71 (1.10;2.64)	1.74 (1.11;2.73)
Change in weight-for-age z-score in Interval 2						
	n=606 p=0.2[c]	n=606 p=0.2[c]	n=626 p=0.3[c]	n=626 p=0.2[c]	n=563 p=0.02[b]	n=563 p=0.02[b]
Catch-down growth	1	1	1	1	1	1
Normal growth	1.08 (0.72;1.62)	1.09 (0.73;1.63)	1.42 (0.94;2.15)	1.44 (0.96;2.16)	1.11 (0.76;1.61)	1.10 (0.76;1.60)
Rapid growth	1.53 (0.89;2.61)	1.51 (0.89;2.56)	1.34 (0.67;2.67)	1.35 (0.67;2.70)	1.92 (1.22;3.03)	1.98 (1.26;3.10)
Growth in weight-for-age z-score in both intervals						
	n=466 p=0.01[c]	n=466 p=0.01[c]	n=508 p=0.3[c]	n=508 p=0.3[c]	n=469 p=0.01[c]	n=469 p=0.01[c]
Never rapid growth	1	1	1	1	1	1
Rapid/no rapid	1.82 (1.19;2.78)	1.81 (1.17;2.80)	1.37 (1.00;1.88)	1.38 (1.00;1.90)	1.55 (1.05;2.29)	1.54 (1.05;2.28)
No rapid/rapid	1.76 (0.76;4.09)	1.73 (0.75;3.97)	1.14 (0.47;2.76)	1.20 (0.49;2.89)	1.89 (1.13;3.14)	1.92 (1.14;3.23)
Always rapid growth	2.87 (1.54;5.34)	2.85 (1.52;5.35)	1.21 (0.44;3.30)	1.21 (0.43;3.45)	2.07 (1.03;4.18)	2.16 (1.04;4.46)
	Weight-for-age z-score at 19.4 months					
Change in weight-for-age z-score in interval 2						
	n=584 p=0.01[c]	n=584 p=0.01[c]	n=602 p=0.05[b]	n=602 p=0.05[b]	n=610 p=0.001[b]	n=610 p<0.001[b]
Catch-down growth	1	1	1	1	1	1
Normal growth	0.73 (0.43;1.24)	0.73 (0.43;1.24)	1.57 (1.04;2.36)	1.57 (1.05;2.36)	1.37 (0.99;1.91)	1.42 (1.02;1.97)
Rapid growth	1.35 (0.73;2.48)	1.37 (0.75;2.48)	1.39 (0.66;2.92)	1.40 (0.66;2.97)	2.14 (1.40;3.26)	2.37 (1.55;3.60)
Change in height-for-age z-score in Interval 2						
	n=582 p=0.01[b]	n=582 p=0.01[b]	n=605 p=0.003[b]	n=605 p=0.003[b]	n=610 p=0.003[b]	n=610 p=0.002[b]
Catch-down growth	1	1	1	1	1	1
Normal growth	1.52 (0.65;3.56)	1.49 (0.62;3.56)	1.22 (0.76;1.98)	1.24 (0.76;2.02)	1.42 (1.01;2.00)	1.43 (1.02;2.01)
Rapid growth	2.25 (0.94;5.40)	2.24 (0.91;5.52)	2.38 (1.38;4.09)	2.38 (1.37;4.15)	2.30 (1.40;3.79)	2.34 (1.46;3.77)

To be continued

Table 4 continuation

Variable	First tertile		Second tertile		Third tertile	
	Crude PR (95% CI)	Adjusted[a] PR (95% CI)	Crude PR (95% CI)	Adjusted[a] PR (95% CI)	Crude PR (95% CI)	Adjusted[a] PR (95% CI)
	Weight-for-height z-score at 19.4 months					
Change in weight-for-height z-score in interval 2						
	n=593 p=0.5[c]	n=593 p=0.5[c]	n=601 p=0.8[c]	n=601 p=0.8[c]	n=600 p=0.01[b]	n=600 p=0.02[b]
Catch-down growth	1	1	1	1	1	1
Normal growth	0.97 (0.46;2.05)	1.00 (0.47;2.11)	1.15 (0.77;1.72)	1.12 (0.74;1.68)	1.11 (0.83;1.48)	1.08 (0.61;1.48)
Rapid growth	1.22 (0.55;2.68)	1.25 (0.56;2.75)	1.16 (0.68;1.98)	1.17 (0.68;1.99)	1.82 (1.26;2.63)	1.83 (1.26;2.66)

[a] Adjusted for family income
[b] Wald test for linear trend
[c] Wald test

Our findings provide input supporting the importance of preventing overweight or obesity during early childhood and maintaining a "normal" growth pattern. Rapid growth during childhood is associated with short-term benefits such as lower risk of hospital admission and lower mortality,[23] but it appear to be a risk for health outcome in the long run.[11,17,19,21] Moreover, accelerated growth should be taken into account when following up "healthy" children in preventive medicine.

The present findings suggest that early experiences may partially determine later health outcomes and are consistent with a life course approach.[2,18]

The mean age of menarche found in the study (12.4 years old) was slightly lower than that reported in other studies in the same city (mean age of 12.7 years in 1991).[15] Unpublished data from a representative study of women in Pelotas in the early 1990s showed that the average age of menarche was 12.8 years among 1,770 women in 2002.

In the early 1990s, the mean age of menarche in Brazil was 13.2 years. It could be argued that these studies did not take into account the year of birth, also known as the cohort effect.[18]

The 1982 Pelotas Birth Cohort Study[24,25] provided good quality of data to the present study. However, there are some limitations: no data on length measurement at birth and no follow-up near menarche age for all girls. Age at menarche was collected retrospectively and in complete years at age 24. Two active birth cohort studies in the city of Pelotas including those born in 1993 and 2004 will allow a more detailed investigation.

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