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How does BMI correlate with menarche onset? Evidence from the Italian HBSC cross-sectional study

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Abstract

Background Menarche is an important period in a female's life; its time of onset may depend on various factors and could correlate with the development of diseases in adulthood. Our study aims to investigate the relationship between body mass index and age at onset of menarche;

Methods We used a unique standardized national dataset on adolescent girls participating in the Italian Health Behaviour in School-aged Children Study. Two independent nationally representative survey datasets: one on 15-year-olds (*n* = 6505, year 2017/2018) and one on 11-year-olds (*n* = 6548, year 2013/2014) were analysed. The survey instrument was the self-report questionnaire. Median age at menarche and 95% confidence intervals were estimated through Kaplan–Meier analysis. Hierarchical models assessed the relationship between BMI and age at menarche;

Results Region-level median age at menarche ranged between 12 years/5 months and 13 years/4 months. Region-level prevalence of overweight among 15-year-old girls ranged between 6% and 24%. Age at menarche was inversely associated with individual BMI (unstandardized regression coefficient beta=-0.81; 95% CI, -0.92 to -0.70). Individual-level and class-level measures of BMI accounted for 215.2% of the region-level variance in age at menarche;

Conclusions The results show that girls who were overweight during childhood went through early puberty. Further investigation needs to assess a possible cause-effect relationship.

Keywords Early puberty, Puberty, BMI, Overweight, Menarche, Obesity

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Background

Adolescence is a crucial phase in the normal development of every person; this period is extremely delicate for young people, as they have not yet learnt how to use those mechanisms and mental processes that are useful for dealing with the challenges and complexities typical of development, so it is necessary to focus more attention on and help adolescents to overcome it by reducing their discomforts, to improve their development. Additional factors, such as pathologies, comorbidities, or ill health status, can further complicate this complex developmental period [1].



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Overweight and obesity are common among children and adolescents. According to United Nations Children's Fund (UNICEF) and World Health Organization (WHO) evaluations, overweight (including obesity) was a global problem in the WHO European Region in 2020, with 4,4 million children under 5 years of age (that represent 7,9% of children in this age group), with wide differences between countries [2].

Obesity is a multifactorial condition characterized by increased adiposity and is associated with an enhanced risk of several non-communicable diseases [3]. Health problems in people living with obesity may derive from the adipose tissue represented in these individuals; it is a metabolically active endocrine organ whose morphofunctional units, the adipocytes, are cells that receive and release hormones [4].

In Italy, more than 40% of children 5–9 are overweight or obese [5], about 20% of adolescents 10–19 are overweight or obese [6]; to measure these data were used the threshold values proposed by Cole et al. in 2000 [7]. There are differences between regions and an increasing geographical gradient from North to South [5, 6, 8]. In line with international data, even in Italy, the same correlation between education level and FAS (Family Affluence Scale) and obesity/overweight subsists [9]. According to recent literature, the increase in the prevalence of overweighted girls may be associated with the age of menarche. Girls with overweight had a higher risk of earlier age at menarche than girls without overweight [10, 11].

The term menarche is used to describe the first menstrual cycle in an adolescent's life and this event marks the beginning of puberty and the entry into childbearing age. It comes later in puberty and is an indicator of sexual maturation. Regarding age, in Italy, menarche usually occurs at a median age of 12,9-year-olds [10].

In early adolescence, obesity significantly impacts health by leading to an earlier onset of puberty, characterized by premature thelarche [12] and menarche [13]. Various theories have been proposed to explain this trend towards earlier puberty, including exposure to environmental toxins and shifts in socioeconomic status. However, it is well-established that nutritional status plays a critical role in the timing and progression of puberty. Despite this, the causal direction of this relationship remains unclear—whether weight gain precedes early puberty, early puberty contributes to abnormal weight gain, or both factors are interrelated [14].

Studies showed that an increase in weight and body mass index (BMI) during childhood correlates with an early onset of puberty [10, 15-17]. So, it is possible to assume that these factors are important in influencing the age of menarche; early onset of menarche has also been correlated with health problems, including breast

cancer, cardiovascular disease, and increased mortality rates in general [15].

Our study aims to correlate the age of onset of menarche with the nutritional status of Italian adolescent girls. The present study is one the first to examine the relationship between obesity and age at menarche by utilising standardised data from all Italian regions, without the problems of interpretation that arise from different methodologies and different cohorts.

Materials and methods

The data presented were obtained from the Italian Health Behaviour in School-aged Children (HBSC) cross-sectional study, following the international HBSC protocol.

All Italian regions were included in the study in order to provide territorially comprehensive coverage. The target population includes all 11-13 and 15-year-old boys and girls inscribed in the first and third grades of lower secondary school and the second grade of upper secondary school. In carrying out the survey, several practitioners were involved and contributed to the work conducted. School principals, classroom teachers, and other school personnel were involved along with local health professionals. Teachers involved in the survey were trained on data collection methods by the Provincial School. Another assignment asked them was to give to the parents, or legal guardian, of each participant the information sheet containing survey details and an optout consent form, to be signed and turned in only if the student declines to participate. Each region employed regional coordinators and Local Health Units (LHUs) to conduct and maintain regionally based activities. The national coordination HBSC 2018 Group, consisting of the National Institute of Health and the Universities of Turin, Siena and Padua, coordinated the activities and performed training sessions on 2018 survey methods for the health workers.

Sampling

Cluster sampling with probability proportional to population size (PPS) was used to obtain a nationally representative sample, with school class as primary sampling unit [18]. More details about this type of sampling method and the main disadvantages are described elsewhere [19]. The Ethics Committee of the Italian National Institute of Health approved the 2018 protocol (PROTPRE876/17, 20 November 201), the protocol also includes the use of an opt-out permission form, in which parents have to explicitly deny consent to their child's participation; failure in returning this signed form was considered as agreement to participation. To preserve the privacy, were adopted all useful procedures to prevent the possible identification of participants, in accordance with European laws [20]. A detailed treatment regarding the purpose, conceptual background, and protocol of the international and Italian study is available elsewhere [21-23].

In the 2017/2018 survey, response rates at school/class level exceeded 85% in most regions [24]. A nationally representative randomized sample of 15-year-old girls (n = 6505) was utilized in order to have regionally comparable data on age at menarche and BMI. The girls were sourced from 1131 schools in the 21 regions that joined the Italian HBSC 2017/2018 survey. Sample sizes ranged from 166 (Valle d'Aosta) to 787 (Veneto). Furthermore, aggregated region-level data on BMI among 11-year-old students (n = 6548) from 1047 schools from 21 of these regions, which had also participated in the 2013/2014 HBSC Italian survey [19], were used. Sample sizes ranged from 182 (Basilicata) to 1046 (Veneto) [25]. We analyzed the prevalence of overweight 15-year-olds girls for all Italian regions and as an aggregate data using 2017/2018 survey data. The same prevalence was also calculated for overweight 11-year-olds girls through data sourced from the 2013/2014 survey to obtain an independent regional figure of overweight levels. The latter group derived from a sample of predominantly pre-menarche girls (75.1%) obtained from the same population of girls who were 11-year-olds in 2013/2014 that was resampled in 2017/2018 at 15 year-olds.

Measures

Information regarding the menarche and age of onset of menstrual cycle was obtained through the following questions: "Have you started menstruating?" the answer to which could be "No, I have not started menstruating yet" or "Yes, I started at the age of ___ years and _ months." The girls were divided into two categories: pre- or postmenstruation. A considerable number of girls were dropped from our analysis due to lack of age at menarche, specifically 2957 girls (31.5%). Self-reported height and weight were used to calculate the Body mass index (kg/m2). When the participants' BMI data were coded, they were then grouped into the following three categories, using WHO age- and sex-specific cut-offs standard deviation of BMI z score's reference: underweight (SD:<-2), normal weight $(-1 \le SD < 1)$, overweight (SD:>1), obese (SD:>2) [26]. In our analyses, we considered students who were categorized "overweight" or "obese" as overweight.

The geographic area of residence was derived from the Region of residence and classified into North, Central and South Italy according to the Italian National Institute of Statistics (ISTAT) classification [27].

Socioeconomic status

Socioeconomic status was evaluated through the Family Affluence Scale (FAS3) [28]. The FAS is a validated measure of material affluence that assigns a composite score on six items: number of family-owned computers (none, one, two or more); having own bedroom (yes/no); number of cars in family (none, one, two or more); number of bathrooms (room with a bath/shower or both) (none, one, two or more); having dishwasher at home (yes/no); holidays with family in the last year (none, once, twice or more). The sum-score can be used to create indices of relative ranks within countries. A useful transformation of the FAS summed score is the ridit transformation of the sum of the scores and then, divides the resulting distribution, as in this case, into three parts of equal size (tertiles, 33% each) obtaining the desired High-Medium-Low classification [29].

Statistical analyses

A continuous variable representing age at menarche was expressed as a median value with 95% CI using the Kaplan-Meier method. A multivariable linear regression model was then used to evaluate the association between BMI and age at menarche among 15-year-olds girls in 2017/2018, adjusted by current age and FAS. The relationship between BMI and age (at menarche) at the individual and region levels was finally assessed through hierarchical models at four levels: individual, school, sampling strata (north, center, south), region. The Model 1 included only age and family affluence; the Model 2 also included individual BMI and the Model 3 included aggregate prevalence of overweight among 11-year-olds in 2013/2014.

The region-level intraclass correlation (ICC), which measures the proportion of the variance in age (at menarche) that is attributable to the region-level, was used. The ICC from Model 2 and Model 3 are expressed as a percentage of the ICC from Model 1, in order to show the change in region-level residual variance. Age at menarche was imputed as current age for those who were premenarcheal. Another regression model was applied to calculate the relationship between the region-wide median age at menarche and the prevalence of overweight among 15-year-olds subjects in 2017/2018 and 11-year-old subjects in 2013/2014. All analyses were carried out using the software SPSS 22.0, Complex Samples module.

Results

The mean age of 15-year-olds in the 2017/2018 survey was 15.5 years (SD = 0.32), and that of 11-year-olds in the 2013/2014 survey was 11.8 years (SD = 0.31). Among 15-year-olds girls with complete menarche data (n = 6505), 1.3% were pre-menarcheal, and the mean FAS score was 8.06 (SD = 2.16).

Differences in the age at menarche were observed among girls and across regions in the sample of 15-yearolds surveyed in 2017/2018. In 95% of individuals, age (at

Region	15 year-	11 year-olds girls (2013/2014)			
	Median	age at menarche	Percentage	Percentage	
	N	Months (years and months)	95% CI (months)	Overweight + obese	Overweight + obese
Abruzzo	340	151 (12 years 6 months)	(149.41-152.59)	12.0	18.6
Basilicata	121	146 (12 years 5 months)	(142.84-149.16)	12.4	21.8
Bolzano	295	155 (12 years 6 months)	(152.53-157.47)	6.3	10.0
Calabria	289	147 (12 years 5 months)	(145.45-148.55)	22.0	25.8
Campania	268	148 (12 years 5 months)	(146.35-149.65)	23.9	34.1
Emilia R.	417	150 (12 years 5 months)	(148.48-151.52)	11.8	18.5
Friuli V.G.	363	152 (12 years 6 months)	(150.32-153.68)	12.9	15.8
Lazio	274	150 (12 years 5 months)	(148.31-151.70)	15.6	18.6
Liguria	282	152 (12 years 5 months)	(149.65-154.35)	10.2	13.2
Lombardy	466	152 (12 years 5 months)	(150.16-153.85)	7.2	12.2
Marche	361	154 (13 years 5 months)	(151.46-156.54)	13.7	18.1
Molise	250	150 (12 years 5 months)	(148.23-151.77)	15.7	19.8
Piedmont	320	151 (12 years 6 months)	(149.26-152.74)	9.6	15.5
Puglia	325	150 (12 years 5 months)	(148.81-151.19)	16.8	34.6
Sardinia	89	150 (12 years 5 months)	(144.64-155.36)	17.9	11.9
Sicily	289	147 (12 years 5 months)	(145.38-148.62)	11.6	23.0
Tuscany	325	151 (12 years 6 months)	(149.50-152.50)	10.1	15.0
Trento	477	155 (12 years 6 months)	(150.15-153.85)	7.0	10.5
Umbria	181	149 (12 years 5 months)	(147.42-150.58)	12.4	17.3
Valle d'Aosta	111	152 (12 years 5 months)	(148.37-155.63)	11.7	16.4
Veneto	662	153 (12 years 6 months)	(151.26-154.74)	12.5	15.3
All regions	6505	151 (12 years 5 months)	(150.59-151.41)	12.5	17.3

 Table 1
 Summary by region of median age at menarche, and percentage "overweight + obese" at age 15 and at age 11. HBSC study, 2017/2018 and 2013/2014

Table 2Linear regression analysis for age at menarche (months)among 15 year-olds. HBSC study, 2017/2018

Independent variables	Unstandardized regres- sion coefficient (β)	95% CI
Body Mass Index (BMI)	-0.75	-0.86 to -0.64
Current age (months)	0.29	0.20 to 0.37
FAS score	0.28	0.13 to 0.42
Constant	111.87	96.18 to 127.54

p < 0.001, age at menarche and current age are measured in months CI = Confidence interval

menarche) ranged between 9 and 15 years and 7 months. No subject was younger than 9 years. The region-level median age (at menarche) ranged from 12 years and 5 months in Marche Basilicata, Campania, Calabria, to 13 years and 5 months in Marche. The region-level prevalence of overweight varied across regions: from 6.3% (Bolzano) to 23.9% (Campania) among 15-year-olds in 2017/2018, and from 10% (Bolzano) to 34.6% (Puglia) among 11-year-olds in the 2013/2014 survey (Table 1).

As shown in Table 2, a significant negative association between individual BMI and age at menarche was observed in 15-year-olds sample. The unitary increase in BMI led to a 1 month earlier onset of menarche (β =-0.75; 95% CI, -0.86 to -0.64). Also considering the single regions (data not showed), without Sardinia, where we have an inverse relation, β =0.40 (statistically not significant p=0.46 CI (-0.66;1.46), menarche occurred earlier in girls with a higher BMI (β ranged from -1.09 to -0.03); however, in six regions, Calabria (β =-0.03 p=0.91 CI (-0.45;0.40)), Lazio (β =-0.42 p=0.10 CI (-0.92;0.08)), Piemonte (β =-0.29 p=0.24 CI (-0.78;0.19)), Puglia (β =-0.32 p=0.14 CI (-0.74;0.11)), Sicilia (β =-0.41 p=0.12 CI (-0.93;0.11)) and Valle D'Aosta (β =-0.73 p=0.11 CI (-1.65;0.18)) this relationship was not statistically significant.

A negative association was observed between aggregate prevalence of overweight and median age at menarche among 15-year-olds in 2017/2018 (Table 3) by treating the regions as units. The median age at menarche was approximately 23 days lower (β =-0.06; 95% CI, -0.07 to -0.06), for each percentage of increase in the region-level prevalence of overweight. As the region-level prevalence of overweight ranged between 6% and 24%, the maximum difference observed in the age at menarche was 79 weeks (approximately 20 months). When the analysis was repeated on region-level data on overweight status among 11-year-olds in 2013/2014, the direction of this relationship was similar (β =-0.23; 95% CI, -0.23 to 0.22).

Table 3	Linear	regression	analysis fo	r region-level	median age a	t menarche am	ong 15-year	-olds in 2017/20	018

Model		Unstandardized regression coefficient (β)	95% Cl
1. 15-year-olds girls 2017/2018	Region-level prevalence of overweight (%)	-0.06	-0.07 to -0.06
	Constant	135.34	135.22 to 135.46
2. 11-year-olds girls 2013/2014	Region-level prevalence of overweight (%)	-0.23	-0.23 to -0.22
	Constant	153.13	153.03 to 153.23

Region-level median age at menarche is measured in months; Region-level of overweight is measured in percent Model 1: Independent variable: prevalence of overweight among 15-year-olds (2017/2018), N=21 regions, p < 0.001Model 2: Independent variable: prevalence of overweight among 11-year-olds (2013/2014), N=21 regions, p < 0.001

model 2. maependent vanable, prevalence of overweight among 11 years

CI = Confidence Interval

Data source: HBSC 2017/2018, HBSC 2013/2014

Table 4 Summary of results from multilevel models of age at menarche (months) among 15-year-olds across 21 regions

Factors	Model 1 adjusted for	Model 2 addition of	Model 3 addition of	
	structural covariates	individual BMI	region-level overweight	
FIXED EFFECTS (95% CI)				
Individual level				
Family affluence Scale (FAS)	0.25 (0.09 to 0.41)*	0.17 (0.01 to 0.32)*	0.17 (0.01 to 0.32)*	
Current age (months)	0.13 (0.04 to 0.21)*	0.14 (0.06 to 0.23)*	0.14 (0.06 to 0.23)*	
Body mass index (BMI)	-	-0.81 (-0.92 to -0.70)*	-0.81 (-0.92 to -0.70)*	
Region level				
Prevalence of overweight (%) of 11 year-olds in 2013/2014	-	-	-0.05 (-0.18 to 0.08)	
RANDOM EFFECTS (SE)				
Region-level variance	0.29 (0.55)	0.59 (0.64)	0.88 (0.85)	
Region-level ICC as percentage of model 1 ICCa	100%	211.4%	315.2%	
Strata-level variance (north-center-south)	3.05 (3.30)	2.24 (2.56)	1.45 (2.46)	
School-level variance	16.39 (2.06)*	17.11 (2.10)*	17.08 (2.10)*	
Residual (individual level) variance	5163.33 (99.47)*	4969.90 (95.89)*	4969.91 (95.89)*	
Log likelihood	-26543.51	-26444.09	-26445.74	
Likelihood-ratio test for change in log likelihood		<i>p</i> < 0.001	<i>p</i> < 0.001	

Age at menarche is measured in self-report age in months, or current age for pre-menarcheal girls

Model 1: Adjusted only for current age and FAS

Model 2: Adjusted for individual BMI measure in addition to current age and FAS

Model 3: Adjusted for region-level prevalence of overweight (%) among 11-year-olds in 2013/2014, in addition to individual-level BMI, current age and FAS CI = Confidence Interval

^aRegion-level Intraclass Correlation Coefficient (ICC) measures the proportion of observed variation in age at menarche attributable to region level

*p < 0.05 significant result for Fixed or Random Effect

To evaluate the association between BMI and age at menarche multilevel regression models were used. No significant differences in age at menarche emerged among the regions; only the coefficient of current age and FAS differed significantly (Table 4: Model 1). In the second model, in addition to the significant difference in the coefficient of current age, region-level variance in age at menarche, increased the ICC by 111.4%, for each unit increase in BMI, age at menarche was approximately and significantly1 month lower (p < 0.001, CI (-0.92; -0.70)) (Table 4: Model 2). In the third model, the fixed-effect estimates did not change, but accounted for a further 215.2% of region-level ICC in age at menarche (Table 4: Model 3). In this final model, for each unit increase in BMI at the individual level, menarche occurred approximately 1 month earlier (β =-0.81; 95%CI, -0.92 to -0.70). In all three models, the school-level coefficient proved significant (Table 4); thus, age at menarche varied with BMI, but in a different way among schools. This variation was not significantly different among regions, nor at the strata level (North, Center and South).

Discussion

As already pointed out by other authors furthermore were observed significant variations in age at menarche across European and North American countries, Italy and Portugal showed the lower values for age at menarche [30], our data show that the mean age at menarche differs by at least 1 year also between the Italian regions. In literature different studies show the correlation between overweight/obesity and early puberty in girls [16, 31–33].

Recently, the decreasing rate of the age of menarche in industrialized countries differs among countries, and this may be linked to the variation in the prevalence of obesity [34]. An European study supported the hypothesis that there is a positive relationship among lowering age at menarche and being overweight [35]. Our work contributes to increasing knowledge regarding this hypothesis as well. In accordance with the results of the previous Italian 2013/14 HBSC in Italy [36], also the 2017/18 survey found a five-fold difference in the prevalence of overweight among 15-year-old girls in all Italian regions. The highest rates of overweight were observed in central and southern Italy, while the lowest rates were seen in northern regions. In particular, the lowest median ages at menarche were observed in southern regions (e.g., Calabria and Campania), where the predominance of overweight is higher.

Longitudinal studies suggest that BMI is one of the risk factors influencing the development of early puberty [17, 35, 37]; this is in accordance with the inverse association between BMI and age at menarche found at individual and class level in our study.

Two different strands of thought can be identified in the literature regarding the correlation between obesity and the time of menarche onset: there is a direct link between leptin, gonadotropin and puberty timing [38], and early puberty is the leading factor in the development of later obesity [34].

Our view is related to the first of the two proposed hypotheses, but it is possible that there is a crosstalk between the theme whereby a redundancy in effects is created.

Furthermore, given the possible influence of some genes on the menarche-overweight association demonstrated by some authors [39], the influence of genetic and environmental factors needs to be studied in more detail.

Adolescence, in both genders, is described as a complex developmental period as multi-factor acts together to induce and promote ponderal excess status (dietary habits, sedentary, genetic, and environment) [40]. In girls, this effect is strongly present due to the increase in estrogen, leading to enhanced insulin resistance [41].

The study has some limitations, such as the study's cross-sectional nature and the self-reported information. BMI which is the epidemiological benchmark indicator is mostly used to measure overweight and obesity [19, 24, 26]. It is important to note that BMI, as a "population study" index, is not able to evaluate the real body composition, as well as it does not allow us to know the distribution of body fat across the subject. Therefore, people with considerable the same BMI may have considerably different fat mass [42]. Higher BMI is not necessarily associated with increased fat mass (e.g., a bodybuilder might present a high BMI but low-fat mass and still be categorized as overweight or obese). However, even though the girls made a bias against their BMI due to excessive

emotional sensitivity toward their weight, there is no recorded bias in the correlation between this data and the age of menarche onset, because going to correlate the remembered age and the effective age of menarche are highly related, particularly when the recall is closer to the age of menarche [43, 44].

Our work, thanks to data collected using a standardized methodology, helps to present up-to-date data about the association between adolescent obesity and menarche onset across Italian regions.

Although the study has those limitations, it has gained new knowledge about the timing of menarche on a representative sample of Italian girls. In addition, the girls involved in the survey were closer to the menarche thus reducing the recall bias and increasing the value of these data at the time of the menarche, thus limiting the memory bias and increasing the value of these data. Premenarchal age girls were included in hierarchical models equalizing the age at menarche with the present one. This comparatively precautionary procedure involved only a few cases (1.3% of 15-year-olds girls were pre-menarche) was used to prevent strengthening the correlation between increased BMI and lower age at menarche. This also allowed us to optimize e the number of girls involved in the study.

Conclusions

Our study confirms the association between early menarche and overweight/obesity based on data from a national surveillance program employing standardized methodologies. Given the robustness of this approach and the need for further investigation, we suggest expanding the analysis to include a comparison of nutritional data and age of menarche among girls from all European countries participating in this surveillance program. This broader comparison could provide valuable insights into the consistency and variability of this association across different populations.

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Author contributions

G.L., D.L., D.M. conceptualized and designed the study; A.P. analysed the data. G.L., D.L., D.M.; wrote the first draft. P.N., R.S., P.D. and A.V; critically reviewed the manuscript and approved the final version. All authors have read and agreed to the published version of the manuscript.

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Data availability

The data presented in this study are available in accordance with the Italian HBSC data access policy. Requests should be directed to paola.nardone@iss.it, member of the National Centre for Disease Prevention and Health Promotion, Italian National Institute of Health.

Declarations

Ethics approval and consent to participate

The study was conducted according to the guidelines of the Declaration of Helsinki. In 2018, the Italian HBSC study protocol and questionnaire were formally approved by the Ethics Committee of the Italian National Institute of Health (Ref. PROT-PRE876/17, 20 November 2017).

Consent for publication

Not applicable.

Informed consent

Informed consent was obtained from all the subjects involved in the study. The data collection was anonymous, and no directly identifiable information on individual pupils were collected. Consent was also obtained by the pupils, who were reminded verbally and in writing that participation was voluntary.

Conflict of interest

All authors declare that they have no conflict of interest.

Competing interests

The authors declare no competing interests.

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