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Body Mass Index and Blood Pressure Pattern through Menarcheal Age in an Italian Village

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Authors' contributions

This work was carried out in collaboration between all authors. Author VM designed the experimental protocol and organized the team for data collection. Author FC projected and computed statistical analysis. Authors ALL and AL wrote the manuscript. All authors discussed results and manuscript and approved the final version.

Original Research Article

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ABSTRACT

Aims: Recent investigations correlated early menarche to cardiovascular risk factors in adulthood, whereas others underlined relationship of menarcheal age to body mass index (BMI) and dysmetabolic conditions. Our aim was to assess whether early menarche could indicate an increased risk factor for enhanced blood pressure and/or hypertensive-range values (systolic/diastolic blood pressure beyond the 95th percentile) within the narrow window of the sexual maturation, 12y to 14y.
Methodology: 463 Caucasian Italian girls were studied at both 12y and 14y: body height (BH), weight (BW), BMI, systolic-diastolic blood pressure (SBP, DBP), presence-absence of menarche were recorded.
Results and Discussion: Lowest quartile for BH, BW, BMI in 12y girls was associated with lower probability (~-20%) of having menarche before 14y. Conversely, girls who

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developed menarche before 12y, at 12y showed higher average BH, BW, BMI, SBP/DBP values versus girls who developed menarche after 12y (about +3.2%;+16.2%;+8.8%;+5.5%;+9.2%, respectively). However, 14y girls of all groups showed similar average SBP and DBP and similar prevalence for hypertensive-range values. Interestingly, at 12y BMI was correlated to hypertensive values of both 12y and 14y (χ^2=17.5; χ^2=15.9; respectively; P<.001). Regression analysis showed that unitary increase of BMI at 12y yielded an increase of 1.04 mmHg for SBP and 0.55 mmHg for DBP in 14y girls.

Conclusions: Early menarcheal age (before 12y) was accompanied by higher SBP and DBP at 12y, but also by higher BH, BW and BMI, versus girls with menarche after 12y. However, early menarcheal age did not influence average SBP/DBP and prevalence of hypertensive-range values in 14y girls. BMI was strongly related to menarcheal status at both 12y and 14y, thus indicating that within this age (12y to 14y) BMI influenced both menarcheal triggering and blood pressure. Further investigations are needed to verify whether cardiovascular risk factors are influenced also in adult age by early menarche, or by high BMI at 12y-14y.

Keywords: Body mass index, body height, body weight, hypertensive values, pubertal age.

ABBREVIATIONS

BH: Body height; BMI: body mass index; BP: blood pressure; BW: body weight; DBP: diastolic blood pressure; NN: menarche after 14 years old; NY: menarche between 12 and 14 years; YY: menarche before 12 years; SBP: systolic blood pressure;

1. INTRODUCTION

Adolescence has been described as a sensitive period for the development of increased risk factors for hypertension in the adult [1]. In particular, early menarche has been associated with several reproductive and cardiovascular risk factors in adulthood, including obesity and hypertension [2-4]. With the onset of sexual maturation both systolic (SBP) and diastolic (DBP) blood pressure increase: according to Daniels et al. [5] age, race, stage of sexual maturation, height, and body mass index (BMI, expressed as kg/m^2) had all significant univariate association of systolic and diastolic blood pressures in longitudinal regression analyses. According to Koziel et al. [6], relative weight is the most important factor related to SBP independently of chronological age and maturity status, whereas height and age of menarche are significantly associated with DBP; height of 14-year-old girls shows the same strength of association with SBP and DBP, whereas maturity status negatively correlates with DBP.

One topic related to adolescent age in our opinion deserves further investigation, i.e., how much the evolution observed in some physiologic parameters (body height, body weight, BMI and blood pressure), in adolescent girls is dependent on the appearance of menarche. We hypothesized that further knowledge of body physiological parameters evolution in parallel with blood pressure and with menarcheal appearance during this age could help anticipating further evolution of the same parameters of adult age. Therefore, we studied: 1) whether the appearance of menarche could produce an increased risk for enhanced blood pressure and/or hypertensive-range values (in this paper hypertensive-range values are defined as those values beyond the 95th percentile for SBP or DBP or both, in our population at their reference age, as described in our experimental conditions - see

Methods); 2) whether blood pressure could show any relationships to body physiological parameters within the narrow window of the sexual maturation, 12y to 14y.

In the present paper we studied the variation of weight (BH), height (BH), BMI and blood pressure (SBP,DBP) in function of the menarcheal condition, i.e., in girls who had either early menarche, before 12y (YY), or late menarche, after 14y (NN), or menarche between 12y and 14y (NY).

2. MATERIALS AND METHODS

2.1 Data Collection

Methods and data collection were described in a previous paper [7]: 463 girls, all caucasians participated in the study. Two complete sets of measurements were collected for all of them, at 12y and 14y. Measurements were performed within the school, following a research protocol approved by school authorities; all adolescents returned questionnaires, filled and signed by at least one parent.

Adolescents lived in and around Albano Laziale, which is a small town (about 30,000 inhabitants), 26 km south-east of Roma, in the zone ‘Castelli Romani’. The territory covers 8 junior high schools, with adolescents aged 11 to 14 years. Our longitudinal investigation

was directed only to those adolescents who, at the time of the first measurement were in the 1st grade, and were between 11 years 6 months, and 12 years 6 months, and 2 years later were in the same section, 3rd grade. All data were obtained between April 1st to May 31st. Standard protocol included:

1) BP measurement. BP was measured twice at 12y and 14y, according to previously established protocols [7] with a mercury sphygmomanometer between the first Korotkoff sound and the fifth Korotkoff sound. The measure was performed after 10 min of quiet sitting, and repeated 5 min later. The second measure of the day was used for further elaborations.

2) BW, approximated to the next 100g
3) BH, approximated to the next 0.5cm.
4) BMI, computed as body weight divided by squared height (kg/m^2).
5) Questionnaire filled by parents, including personal data and menarcheal condition, family data, number and degree of relatives suffering with hypertension, diabetes or both, including uncles and grand parents (2nd degree relatives).

2.2 Statistical Analysis

Categorical variables have been synthesized as absolute and percent frequencies, while continuous variables have been summarised using means and standard deviations. In addition, for the latter age-specific percentiles have been computed to make the results comparable with those from other investigators. Due to the high number of ties (observations with equal values) in the distribution of each variable, percentiles only approximately divide the total frequency of the sample into the desired proportions.

Adolescents with SBP and/or DBP (any of the two, or both) greater than or equal to the corresponding 95th percentile were defined as "hypertensive", whereas those with both SBP and DBP less than the corresponding 95th percentile were defined as "normal". The term "hypertensive" here is not used in the clinical meaning of the word, also because BP values can shift from 95th percentile to 90th percentile and vice-versa. Differences in weight, height, and BMI between groups of adolescents were tested by Student t test.

Association between categorical or categorised variables was tested using the " χ^2 " test.A multiple linear regression model was applied to assess the contribution of weight, height and BMI (independent variables) at 12 years of age on SBP and DBP (dependent variables) at 12 and 14 years of age.

Linear regression analysis was performed in order to assess the effect of potential prognostic factors on systolic or diastolic blood pressure at 14 years of age (different analyses for the whole group of adolescents and for the different subgroups based on menarcheal condition). Regression coefficients with 95% confidence intervals were computed for the variables included in each model.

3. RESULTS

3.1 Description of Variables in 12y and 14y Girls, with Reference to Overweight and Obesity

All 463 girls were examined at both 12y and 14y, as said. Distribution of variables at 50, 90 and 95 percentiles in 12y and 14y girls, respectively, are shown in Table 1. Absolute number of girls at or above the 95th percentile is indicated in parenthesis.

Table 1. 12 and 14 years old girls: distribution of percentiles

Parameter	**12 years old girls**				**14 years old girls**			
Percentiles	**50th**	**90th**	**95th**	**(n)**	**50th**	**90th**	**95th**	**(n.)**
Weight (kg)	46.6	58.5	65.1	(23)	53.5	66.2	73.0	(24)
Height (cm)	152.3	160.0	163.4	(30)	159.6	167.1	169.4	(39)
BMI (kg/m^2)	19.2	24.1	26.0	(31)	21.1	25.0	27.2	(35)
SBP (mmHg)	107.0	125.0	145.0	(19)	110.2	130.4	140.0	(34)
DBP (mmHg)	65.0	76.0	85.0	(32)	65.8	80.0	85.1	(36)

Values of the various parameters in percentiles, at 12y and at 14y. The values in parenthesis show the absolute number of girls belonging to the 95th percentile. Blood pressure values at or beyond the 95th percentile were classified in this investigation as "hypertensive-range values".

3.2 Association between BMI and Hypertensive-Range Values at 12y and at 14y

Association between overweight (BMI > 90th percentile) and hypertensive-range values (i.e., SBP or DBP or both ≥95th percentile) was found in our girls at both ages (Table 2A and 2B). Data show a consistent increase of hypertensive-range values in correlation to BMI at both ages. Moreover, BMI distribution in 12y girls indicated highly consistent association with hypertension at 14 years, as well (Table 2C.).

Table 2. Relationship between BMI and hypertensive-range values at 12y and 14y
Table 2A. BMI and girls with hypertensive-range values at 12y

BMI range at 12y	Percentile of BMI	SS with normal values N	(%)	SS with Hypertensive-range values N	(%)	Total
10 to 19.9	≤50^{th}	204	(94.0)	13	(6.0)	217
20 to 24.9	51^{th} -90^{th}	181	(91.0)	18	(9.0)	199
≥25	>90^{th}	35	(74.5)	12	(25.5)	47
χ^2 = 17.5; d.f. = 2; *P*< .001						
Not overweight		311	(93.1)	23	(6.9)	334
Overweight		109	(84.5)	20	(15.5)	129
χ^2 = 8.2; d.f. = 1; *P*= .004						
Not obese		406	(91.9)	36	(8.1)	442
Obese		14	(66.7)	7	(33.3)	21
χ^2 = 15.1; d.f. = 1; *P*< .001						
TOTAL		420	(90.7)	43	(9.3)	463

Table 2A. Girls showed increased percentage of hypertensive-range values with increasing BMI values, i.e., in 12y girls a percentage of 6.0% with BMI <20, showed hypertensive-range values, versus 9.0 and 25.5% in girls with BMI respectively between 20 and 25 and BMI >25. Similarly, 6.9% non-overweight girls showed hypertensive-range values, versus 15.5% in overweight; and 33.3% obese girls showed hypertensive-range values (P at least =.004) (numbers indicate absolute number of girls; percentage between brackets)

Table 2B. BMI and girls with hypertensive-range values at 14y

BMI range at 14y	Percentile of BMI	SS with normal values N°	(%)	SS with Hypertensive-range values	(%)	Total
10 to 21.9	≤50^{th}	248	(94.3)	15	(5.7)	263
22 to 25.9	51^{th} -90^{th}	127	(83.6)	25	(16.4)	152
≥26	>90^{th}	33	(68.7)	15	(31.3)	48
χ^2 =29.8; d.f. = 2; *P*< .0001						
Not overweight		329	(91.9)	29	(8.1)	358
Overweight		79	(75.2)	26	(24.8)	105
χ^2 = 21.5; d.f. = 1;*P*< .001						
Not obese		398	(88.8)	50	(11.2)	448
Obese		10	(66.7)	5	(33.3)	15
χ^2 = 6.8; d.f. = 1; *P*= .009						
TOTAL		408	(88.1)	55	(11.9)	463

Data show the same trend as data in Table 2.A

Table 2C. BMI distribution of 12 years old girls, and indication of association with hypertensive-range values at 14 years

BMI range at 12y	Percentile of BMI	SS with normal values at 14y	(%)	SS with Hypertensive-range values at 14y	(%)	Total
10 to 19.9	<50th	205	(94.5)	12	(5.5)	217
20 to 24.9	51th -90th	165	(82.9)	34	(17.1)	199
≥ 25	>90th	38	(80.9)	9	(19.1)	47
χ^2 =15.9; d.f. = 2; *P*= .0004						
Not overweight		305	(91.3)	29	(8.7)	334
Overweight		103	(79.8)	26	(20.2)	129
χ^2 = 11.7; d.f. = 1; *P*= .001						
Not obese		393	(88.9)	49	(11.1)	442
Obese		15	(71.4)	6	(28.6)	21
χ^2 = 5.9; d.f. = 1; *P*= .02						
TOTAL		408	(88.1)	55	(11.9)	463

3.3 Conversely, Consistent Correlation between Hypertensive-Range Values and Menarcheal Condition was not Found

In Tab 3 the absolute number (and the percentage) of girls in the three menarcheal conditions (NN+NY+YY) are shown versus number (and percentage) of girls with hypertensive-range values at 14y. Note that percentage of girls with hypertensive-range values does not differ consistently among the three groups (Pearson's χ^2 = 2.8; d.f.= 2; *P*=.250 (ns). Although differences are not significant among groups, yet in the YY group only 6.7% of 14y girls show hypertensive-range values. As a further datum, we computed also the relationship between hypertensive-range values in YY girls *versus* NY and NN girls cumulated (Pearson's χ^2=2.32; d.f.=1; P=.127 (ns)). This datum waits for further corroboration, before any hypothesis can be forwarded (see also the Conclusion chapter).

Table 3. No relationship among menarcheal condition and hypertensive-range values at 14y

Menarche	Hypertensive-range values			
	Normal (%)	Hyper. Val. (%)	Total (%)	In %
NN	74 (16.0)	13 (2.8)	87(18.8)	13/87 = 14.9 %
NY	264(57.0)	37(8.0)	301(65.0)	37/301 = 12.3 %
YY	70 (15.1)	5 (1.1)	75(16.2)	5/75 = 6.7 %
TOTAL	408(88.1)	55 (11.9)	463(100)	

Relationships among menarcheal condition and hypertensive-range values at 14 years in the 3 groups. The percentage of girls with hypertensive-range values at 14 years does not show any relationship to menarcheal condition. Pearson χ^2 = 2.8; d.f. = 2; P= .250 (ns). However, please note that girls with early menarche show lower percentage of hypertensive-range values (6.7%), versus other groups cumulated (13%), even if the difference is not statistically significant (YY girls versus NY and NN cumulated: Pearson's χ^2 = 2.32; d.f. =1; P= .127 (ns).
Menarche NN means: No menarche at 12y and No menarche at 14y; NY means No menarche at 12y and menarche at 14y; YY means menarche at/before 12y
Hypertensive-range values in the first line means: among a total of 87 girls who did not have menarche at 12 and 14y, 74 of them did not show hypertensive-range values at 14y. The same holds true for the following lines

3.4 BW, BH, BMI, SBP and DBP Progression in 12y and 14y Girls in the three Menarcheal Conditions. At 14y, all Groups Show Analogous Mean SBP and DBP

Table 4A and 4B show mean values for said parameters of 12y and 14y girls, respectively in relation to menarcheal condition. At 12y, the mean values of parameters of girls in YY condition was in general consistently above the values of other girls, as expected (Table 4A). However, at 14y all girls reached similar blood pressure values, unrelated to menarcheal age (Table 4B). In this case, the mean values of height, weight and BMI in NN girls were consistently below the values recorded in NY and YY girls.

Table 4. Body physiologic and blood pressure parameters in 12y and 14y girls, belonging to the three menarcheal conditions

Table 4A. 12 years old girls

Parameters	Menarcheal condition		
	NN	NY	YY
Height (SEM)	148.9(0.8)***	152.7(0.4)***	155.7(0.6)
Weight (SEM)	41.1(1.0)***	47.5(0.6)**	51.5(1.1)
BMI (SEM)	18.5(0.3)***	20.2(0.2)	21.1(0.4)
SBP (SEM)	108.4(1.6)	110.1(0.9)*	115.3(2.1)
DBP (SEM)	63.1(1,3)	65.2(0.6)**	70.1(1.2)

Table 4B. 14 years old girls

Parameters	Menarcheal condition		
	NN	NY	YY
Height (SEM)	158.4 (0.7)*	160.5 (0.3)	160.8 (0.6)
Weight (SEM)	50.8 (1.0)**	56.0 (0.5)	58.1 (1.0)
BMI (SEM)	20.2 (0.3)***	21.6 (0.2)	22.4 (0.4)
SBP (SEM)	114.7 (1.5)	115.4 (0.8)	114.3 (1.5)
DBP (SEM)	71.2 (1.1)	71.1 (0.6)	72.6 (1.1)

*Physiological parameters in 12y (Table 4A) and 14y girls (Table 4B), classified according to their menarcheal condition. NN, NY and YY as in Table 4 for the appearance of menarcheal condition (mean ± SEM). * is for P< .05; ** is for P<.01; *** is for P<.001*

In this Table in all cases significant difference between contiguous values in the same line means also significant difference versus the non contiguous group. For example: for 12y girls SBP is higher in YY group (115.3) versus NY (110.1), and is also higher versus NN (108.4), while in the same line the mean of NY group is not different from NN. Please note that 14y girls in the three groups show the same average blood pressure, for both SBP and DBP.

3.5 A Consistent Correlation Was Found Between BMI and Blood Pressure

The regression analysis performed to evaluate the prognostic role of different factors on blood pressure at 14y of age, pointed to a significant effect of BMI at 12y of age on SBP and DBP at 14y in the overall group of girls. Specifically, a unitary increase of BMI at 12y yielded an increase of 1.04 mmHg for SBP and of 0.55 mmHg for DBP in the whole group of 14y girls, while in the subgroups these values ranged from 0.82 to 1.81 for SBP and from 0.49 to 0.72 for DBP (see Table 5A and 5B for details).

Table 5. Relationship between BMI at 12y and blood pressure at 14y

Table 5A. Systolic blood pressure at 14y

SBP at 14y	Coefficient	SEM	t	p
Whole group	1.04	0.1852	5.60	0.000
NN subgroup	1.81	0.4551	3.99	0.000
NY subgroup	0.82	0.2323	3.53	0.000
YY subgroup	1.17	0.4113	2.84	0.006

Table 5B. Diastolic blood pressure at 14y

DBP at 14y	Coefficient	SEM	t	*P*
Whole group	0.55	0.136	4.04	0.000
NN subgroup	0.72	0.331	2.18	0.032
NY subgroup	0.49	0.169	2.90	0.004
YY subgroup	0.71	0.328	2.16	0.034

Association between BMI at 12y, and blood pressure in the whole sample and for each menarcheal condition at 14y. In the whole group of 14y girls a unitary increase of BMI at 12y yielded an increase of 1.04 mmHg for SBP and of 0.55 mmHg for DBP, while in the subgroups these values ranged from 0.82 to 1.81 for SBP and from 0.49 to 0.72 for DBP (data in bold characters. SEM is for standard error; t and P are referred to statistical significance)

3.6 The distribution in Quartiles of BW, BH and BMI at 12y was Related to the Probability of having Menarche before 14y

Data in Fig. 1 indicates that girls with height or weight or BMI in the lowest quartile at 12y have a lower probabilità of having menarche at or before 14y. 12y girls with height in the lowest quartile (up to 147.5cm) or weight (up to 39.9kg) or BMI (up to 17.1kg/m^2) have respectively a probability of 67.9; 67.2 and 73.1% to gain menarcheal condition between 12y and 14y of age, versus 84.8 to 93.3% of girls who belong to the higher two quartiles. Thus, girls who have early menarche show also higher height, weight and BMI.

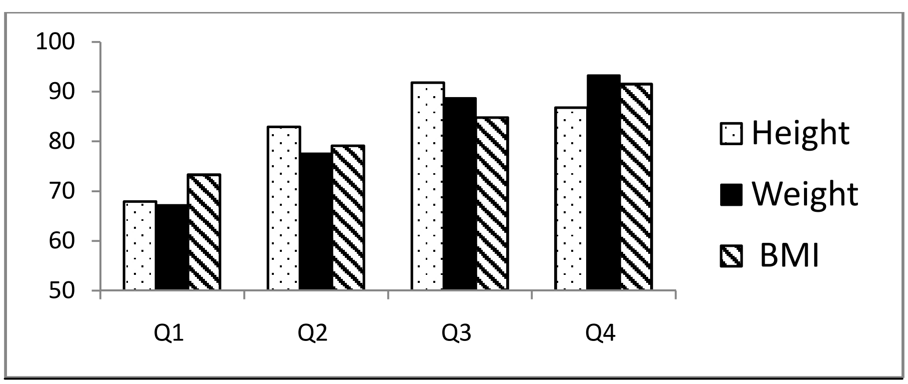

Fig. 1. Relationship between distribution of physiologic parameters in quartiles at 12y, and probability of developing menarche within the two following years

Ordinate: percent of menarche in girls at 14y; abscissa: quartiles of BW, BH and BMI at 12y. The higher is value for any of the three parameters, the higher is probability of developing menarche before 14y. The probability of having menarche increases strongly for girls in the higher quartiles (for body weight, Pearson's $\chi 2$ = 22.1, P = .0001. For BMI, Pearson's $\chi 2$ = 25.3, P = .0001)

4. DISCUSSION

4.1 Description and Reliability of the Experimental Population

Present data confirm and extend our previous information published on a population of both male and female adolescents [7], and are compatible with previous data published for Italian populations [8,9]. Although several normative data were published in various countries, results may depend in function of a number of variables, including the regions within each country. For example, according to Cole et al. [10] cut-off point for overweight in adult women is at 90th percentile and cut-off point for obesity is at the 95th percentile in a given population. At 12y these BMI cut-off points for overweight in girls corresponds at 21.7 kg/m², and at 14y is 23.3kg/m², In our population data is somehow different: these points correspond approximately at the 75th percentile, at either age (Table 1).

For obesity, BMI cut-off points in [10] was 26.7 and 28.6, respectively. In our population the BMI 95th percentile in12y girls is 26.0, whereas the 95th percentile for BMI in our 14y girls is 27.2. Recent paper [9] studied a population in the southern Italy with BMI and DBP quite analogous to ours, while average SBP was higher (102 ± 11 SD and 106 ±10 respectively, for 12y and 14y girls). Here, for all elaborations we adopted percentile data from our own population, which is analogous to data described for Italian girls of the same age [8,9]. For deeper discussion on the topic see also for example Koebnick et al. [11].

4.2 Correlation of BMI with Hypertensive-Range Values

In our population the distribution in classes of BMI at 12y was positively correlated to the number of girls in the hypertensive-range values at both 12y and 14y (Table 2A, 2B, 2C). Moreover, a unitary increase of BMI at 12y yielded an increase of 1.04 mmHg for SBP and of 0.55 mmHg for DBP in the whole group of 14y girls. Our data therefore confirm and extend previous indication for weight control in adolescent girls [11-13] as a powerful preventive intervention to control overweight and risk factors for the development of hypertension in this age. We found also that prevalence of hypertensive-range values increases progressively with increasing BMI, thus confirming and extending previous studies, which detected hypertension in about 30% of overweight children [14] (See also [11]).

4.3 No Relationship between Menarche Timing and Hypertensive-Range Values

In our population no consistent difference was found between the percentage of girls with hypertensive-range values and with early menarche, or with late menarche, or with “normal age” menarche (Table 3), although a lower percentage of hypertensive values appears in girls with early menarche (6.7%). Analogous percentages for hypertensive values (10.7%) were recently published [9]. Therefore, our data suggest that early menarche by itself does not appear to be a risk for the development of hypertensive-range values in adolescent girls within the narrow chronological window we studied. This hypothesis is further enforced by data shown in Tables 4A and 4B. Menarcheal condition appears to influence greatly all parameters listed in Table 4A at 12y only, including blood pressure values which reached a maximum in girls who had menarche before 12y. But at their 14th year, girls of all menarcheal condition had quite analogous average SBP and DBP. Therefore, physiologic evolutions which accompany body changes in adolescent girls may accelerate body parameters and blood pressure increase, but age 14y (in addition to hormonal equilibrium) these changes appear as a limiting factor in the evolution of blood pressure.

4.4 Influence of body Weight, Height or BMI on the Probability of Correlation with Menarcheal Conditions

Girls in the lower BMI, or body weight and height (i.e., in the lowest quartile) show a relatively low probability of having menarche during the two following years (67.6%, 64.3% and 62.0%, respectively), whereas the probability of having menarche increases strongly for girls in the other quartiles, i.e., the probability for 12y girls in the highest BMI quartile of having menarche within the 14^{th} year was 31% higher than girls in the lowest BMI quartile. The influence of higher BW and BMI on menarche appeared to be stronger than the influence of BH. We speculate that the mean increase of BW and BMI between 12y and 14y (17.9% and 7%, respectively) was more intense than relative increase of BH (5.1%).

4.5 Study Limitations

Total number of girls enrolled in the study (463) corresponds exactly to the subjects who performed all required conditions, with all subjects tested twice (at 12 and again at 14 years of age). This procedure has both risks and benefits. From the one hand, our strategy considers exactly the same adolescents in both ages measure, and this may lower the variability of our sample. From the other hand, this procedure brings to “exclude” those cases which are considered only once and cannot be followed longitudinally; moreover, applying this procedure a smaller number of cases are admitted in the study. A point in our working hypothesis was to verify whether risk factors for the development of hypertension could be predictive during this particular age, in the same subjects, with a time delay (2 years), which is limited in itself, but which may give indication for the repeatability of measures, and therefore give a contribution to those strategies aimed at acknowledging and evaluating early risk factors. Moreover, the definition of “hypertensive-range values” may be discussed, because it is based on one occasion only, and may be influenced by factors such as “white coat hypertension”. However, bias was reduced in our case by accurate protocol application, and by measurement repetition. In a recent paper [11] these possible sources of error are discussed.

Our investigation was designed to study the timing *relationships* of three groups of parameters within the critical period of development in women life, i.e., body physiological parameters, menarche, and blood pressure. We showed that, within the narrow period of 12y to 14y, the BMI pattern (and in part BH and BW) is strongly connected to blood pressure evolution. Menarche appearance induce profound modifications of all body parameters and blood pressure, as it is well known, but these modifications depend as a whole also on the age of girls, beyond menarcheal appearance itself and its hormonal equilibrium (we underline that at 14y SBP and DBP are almost identical in the three groups of girls). The inverse relationship was also observed: high BMI at 12y (and also high BH and BW) is strongly indicative of menarcheal triggering before 14y. Our investigation, therefore, does not intend to contribute to the debate on possible association of early menarche with cardiovascular disease in adult women, or, vice-versa, on the association of body parameters with adult cardiovascular disease. We confide that our data may be a contribution to the knowledge of physiological evolution in adolescent girls, taking in consideration the three above said parameters.

Physiological parameters appear of importance for blood pressure monitoring, and overall, BMI value at 12y is strongly associated positively with blood pressure at 12y and at 14y. Moreover, 12y girls with BMI in the lowest quartile show lower probability of developing menarche in the following 2 years, versus girls in the higher quartiles. Therefore, we conclude that an elevated BMI in adolescence may contribute to substantial risk factor for obesity-related disorders in the following years, and control of BMI (and body weight) is a rationale intervention to reduce various indexes of adiposity, and these changes may reduce the risk of childhood-onset type 2 diabetes, whereas women with history of early menarche were described to have higher risk of type-2 diabetes in adulthood [14,15]. Analysis of possible relationship among YY menarcheal condition and hypertensive-range values at 14y would indicate a lower percentage of girls with hypertensive-range values (5/75, i.e., 6.7%) versus all other conditions cumulated (50/388, i.e., 13%) (see Table 4A and Table 3); however, the difference is not significant, therefore we cannot speculate that early menarche in girls with high BMI/BW at 12y is actually protective regarding the risk for hypertension.

5. CONCLUSIONS

In conclusion, we think that the real definition between cause and effect is still to be defined. We started our investigation with a question: is the early menarche the main cause for adult hypertension/high BMI? Or, vice-versa, is high BMI the main cause for early menarche and adult hypertension? Our paper cannot answer this question. In our paper we show that in girls early menarche (<12y, and therefore girls with "mature" hormones levels) is accompanied by high BMI, BH, BW, SBP and DBP, versus all other girls, as expected. However, at 14y body physiological differences among groups are much less evident, and blood pressure is at the same level in all girls (Table 4A and B). Therefore, the effectiveness of early menarche as the main trigger for enduring high blood pressure does not appear of great and enduring importance. Better knowledge of hormone levels, and also knowledge of subtle brain and other organs regulatory/feedback mechanisms could contribute understanding our data, and we still believe that there are many mechanisms we do not still understand within this interesting ontogenetic period. Finally, as Tirosh et al [13] suggested, along with existing guidelines, these findings call for high awareness for pediatricians in using an integrated individualized assessment that incorporates sex and late adolescence BP and BMI in predicting the risk of hypertension in young adulthood, an age group that frequently escapes continuous medical attention.

CONSENT

Not applicable.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exists.

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