

Body Mass Index as a risk factor for early menarche: A case-control Study

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ABSTRACT

INTRODUCTION: The early age of menarche has been linked to several adverse health effects during childhood, such as eating disorders and depression, and during adulthood, such as short stature in the future, increased adult BMI (obesity), early marriage, type II diabetes, metabolic syndrome, breast, endometrial, and ovarian cancers, cardiovascular disease and overall mortality and morbidity in adolescent girls and young women.

OBJECTIVE: Measuring the association between BMI at school entry and at the time of the study with the onset time of menarche.

METHODS: A case-control study was conducted in Baghdad city at nine governmental intermediate schools for girls. Students with early menarche were the cases which was defined as girls getting menarche at the age of 11 years and less. Those who started menarche at a normal or late age were considered the control. BMI was calculated at entry to the school and at the time of the study and compared with early menarche. We also measured the association of early menarche with some social factors.

RESULTS: The study showed that the prevalence of obesity for girls from school entry to the time of the study was 6.4, and being obese is statistically associated with early menarche, p-value =0.001. Girls with early menarche were taller than their peers at the time of the study (p=0.001). Similarly, having a mother or sisters with a history of early menarche and a higher level of education of the parent were associated with a higher chance of getting early menarche.

CONCLUSION: The age of menarche decreases as the BMI increases. Girls with early menarche were taller than others at the time of the study. The age of menarche was significantly associated with the parents' educational level and family history of early menarche for mothers and sisters.

Key words: Early menarche, BMI.

INTRODUCTION

Puberty in girls is a transition period, making physiological development a challenge that adolescents have to face. Early pubertal development could be associated with higher risks of poor health.^[1] Besides, pubertal obesity is considered the most prevalent preventable health problem for puberty worldwide, with significant morbidity and mortality such as endocrine, reproductive disorders, diabetes, cardiovascular diseases, obstructive sleep apnea, osteoarthritis, gastrointestinal disorders, cer-

tain neurological disorders and cancers.^[2]

Early age at menarche is often defined as equal or less than 11 years old.^[3] Girls experience menarche at different ages, and timing varies by geographical region, ethnicity, race, female biology, genetic and environmental factors, especially nutritional factors, higher growth rate during childhood, higher childhood socio-economic level, family conflict-divorce, and exposure to stressors during or shortly before menarche.^[4] Age at menarche reflects numerous health aspects and is con-

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sidered a major risk factor for many diseases in women, including the timing of sexual maturation, growth and nutritional status, and environmental conditions.^[5]

In Iraq, 11.8% of children under five years old were overweight in 2011 and raised to 15.35% in 2012.^[6] The dietary and physical activity behaviours of children and adolescents can be influenced by many sectors of society, including families, schools, child care settings, medical care providers, government agencies, the media, food and beverage industries and entertainment industries.^[7]

Few cross-sectional studies were done in Iraq to address factors associated with age at menarche. A study conducted in Baghdad in 2002 found that family size and BMI can affect the age of menarche.^[8] Another study from Tikrit in 2010 concluded that the mean age of menarche decreases as the BMI increases and is affected by sports, stressful environments and a history of early menarche in a girl's first-degree relative (mothers, sisters).^[9] Descriptive studies from India^[10] and Nigeria^[11] found that girls from the middle or high socio-economic class matured earlier than those from the low socio-economic class. Another study in India showed that place of residence, urban or rural, does not seem to affect the mean age of menarche.^[12] A study in Spain showed that menarche occurs earlier among girls compared to their mothers. This trans-generational shift has been documented in Chile, the United States, Latin America, and Europe.^[13,14]

Early puberty is not without a price; a study done in the USA showed that early puberty was associated with a higher risk of psychological troubles and more likely to join in risky behaviours like smoking and alcohol use.^[15] It has been noticed that white girls were at significantly lower risk of early menarche than black girls.^[16]

The aim of the study is to measure the association between BMI at school entry and the time of study with the onset time of menarche. To compare different socio-economic variables: age, the living and education status of parents, size of the family, and family history of early

menarche in girls who had early menarche to those who had menarche at normal or late age.

METHODS

Setting and study design: a case-control study was conducted in Baghdad city in nine governmental Intermediate schools of different social levels (to overcome the deference in socio-economic status in this study) for eight months from the 24th of April to December 2017.

Ethical consideration: The ethical committee of the scientific board in community medicine at the Iraqi Council for Medical Specialities approved the protocol of this study. Official permission was obtained from the Ministry of Education, the relevant education directorates, and the administrations of the selected schools. Written consent was taken from the parents of the students. The aims of the study were explained to the participants before the start, and data were kept confidential and not to be divulged except for the study purpose.

Definition of the case: All girls in the intermediate classes of the schools selected were the targets of this study. Girls with early menarche, defined as menarche, start at 11 years or less^[3] were considered early menarche cases. Girls from the same schools and classes who started their menarche at 14 years or later^[17] or have not yet gotten it at the time of the conduction of the study were selected as the control group.

Exclusion criteria: We excluded students with a history of chronic diseases such as asthma or diabetes mellitus; using drugs like insulin and sodium valproate; and Girls with precocious puberty, defined as the appearance of physical and hormonal signs of puberty development at an earlier age than eight years.^[18] Girls who refused to participate or had incomplete documented data were excluded from this study.

Sampling methods: We randomly selected three health sectors from Baghdad. Two to three intermediate schools for girls were also randomly selected from each sector. Then, girls in the 1st class of the intermediate school who are 12-13 years old were conveniently chosen

for the interview with the authors. The study was designed to involve intermediate schools rather than primary to avoid difficulties expected from a poor understanding of girls in primary school about the terms of menses and being shy about speaking about these private issues. The sample size was calculated from the open-epi online program.^[19] We used the following to fill the formula: Two-sided confidence was 95%, level (1-alpha) was 80 %, the ratio of controls to cases was 2, the hypothetical proportion of controls with exposure was 40 %, the hypothetical proportion of cases with exposure was 50 %, and least extreme Odds Ratio to be detected 1.5. Accordingly, the total number of cases was 290 students, and the control was 580.

Design of the questionnaire: The authors have designed the questionnaire based on similar studies. Many gynaecologists and community physicians reviewed the questionnaire to make sure that it is valid and understandable.

The authors collected data four days a week with an average of 12 participants daily. After explaining the nature of the questions, students were asked to answer them. Then, the height and weight of each participant were measured to calculate the BMI. The height and weight of the students on entry to the school were taken from students' records kept at the school, and BMI was also calculated. The interview with each student took about 12-15 minutes.

Outcomes: We measure the height and weight of each student at school entry (taken from the school records) and at the time of the study. Time at menarche has also been taken from the students and classified into two groups accordingly. We measure any association between having early menarche and height and weight on school entry, family history of early menarche, and parents' educational levels. The association of early menarche was also measured with other social factors like loss of father due to, for example, death, migration due to violence, or having stressful events in the family like divorce or separation of the parents.

Statistical analysis: We used Microsoft Excel and SPSS version 22 programs in statistical

Table 1 | The distribution of participants by demo-social features in case and control groups

Demo-social features		Cases (n=290)		Control (n=580)	
		No.	%	No.	%
Age	12 years	15	5	70	12
	13 years	275	95	510	88
Family history of early menarche	Mother	54	18.6	19	3.3
	Sister	32	11.0	39	6.7
	Non	204	70.3	522	90.0
Parents living status	Lived together	262	90.3	498	85.9
	Not lived together	28	9.7	82	14.1
Parents loss	Both alive	263	90.6	516	89
	At least one died	27	9.4	64	11
Educational level of father	Primary	118	40.7	211	36.4
	Secondary	92	31.7	275	47.4
	University	80	27.6	94	16.2
Educational level of mother	Primary	62	21.4	174	30.0
	Secondary	114	39.3	264	45.5
	University	114	39.3	142	24.5
Family size	Small family (≤ 4)	86	29.7	196	33.8
	Big family (>4)	204	70.3	384	66.2

analysis. Data were displayed in tables and presented by frequency and percentages. We used the Chi-Square test, t-test, and Odd ratio for analytic statistics. To find out the association between related variables, binary logistic regression was used to determine the most effective variables that may lead to early menarche. A P-value less than 0.05 was considered to be a monitor of significance.

RESULTS

The results of this study showed that 275 (95%) of cases and 510 (88%) of controls were 13 years old. Girls in the cases group have a family history of early menarche for mother or sister in 86 (29.6%), while only 58 (10%) in control groups. Of the total, 262 (90.3%) of girls with early menarche and 498 (85.9%) of the control group lived in families where their parents lived together. About two-thirds, 204 (70.3%), of girls with early menarche had a big family, compared to 384 (66.2%) of the control group. **Table 1** shows the distribution of other participants' demo-social features.

The association between BMI at the time of school entry and current BMI and age of me-

Table 2 | the association between BMI at school entry and BMI at time of study with age of menarche.

Time	BMI	Cases group		Control group		P value	OR	95 % CI	
		N	%	N	%			lower	upper
At school entry	Normal	99	34.1	408	70.3	0.001		Reference	
	Over	54	18.6	128	22		1.73	1.18	2.55
	Obese	137	47.3	44	7.7		12.83	8.56	19.22
At the study time	Normal	113	38.9	379	65.3	0.001		Reference	
	Over	135	46.6	180	31		2.51	1.85	3.41
	Obese	42	14.5	21	3.7		6.70	3.81	6.61

Table 3 | Height status and menarche age association.

Time	BMI	Cases group		Control group		P value	OR	95 % CI	
		N	%	N	%			lower	upper
At school entry	Normal	132	45.5	281	48.4	0.551		Reference	
	Tall	88	30.3	156	26.9		1.20	0.86	1.67
	Short	70	24.1	143	24.7		1.04	0.73	1.48
At the study time	Normal	193	66.5	371	64	0.001		Reference	
	Tall	55	19	58	10		1.82	1.21	2.74
	Short	42	14.5	151	26		0.53	0.36	0.78

narche is shown in **Table 2** and **figure 1**. At the entry to the school, 137 (47.3%) students in the cases group were obese compared to 44 (7.7%) in the control group with an odds ratio of 12.8, 95 % CI (8.56 -19.22), p-value = 0.001. In contrast, 42 (14.5%) of the students in the cases group were obese at the time of the study compared to only 21 (3.7%) in the control group, OR=6.70, 95 % CI (3.81-6.61), p-value

=0.001. The data below shows the calculated prevalence of obesity for girls who were obese and still obese (BMI 1 obese –BMI 2 obese) was 6.4%.

The association between the height of the participants at school entry and the time of study in the cases and control group is shown in **Table 3** and **figure 2**. The table illustrates that

Table 4 | The association between different socio demographic variables and menarche age.

		Cases group		Control group		P value	OR	95%CI
		N	%	N	%			
Educational level of father	Primary	118	40.7	211	36.4	0.0001		Reference
	Secondary	92	31.7	275	47.4		1.67	1.21-2.32
	University	80	27.6	94	16.2		0.66	0.45-0.95
Educational level of mother	Primary	62	21.4	174	30	0.0001		Reference
	Secondary	114	39.3	264	45.5		0.82	0.57-1.18
	University	114	39.3	142	24.5		0.44	0.30-0.64
Family history of early menarche	None	204	70.3	522	90	0.001		Reference
	Mother	54	18.6	19	3.2		0.48	0.29-0.78
	Sister	32	11.1	39	6.8		0.14	0.08-0.24
Size of family	Small family ≤ 4	86	29.6	196	33.7	0.219		0.826
	big family >4	204	70.4	384	66.3			0.61-1.17
Parent loss	both alive	263	90.6	516	89	0.433		1.208
	At least one died	27	9.4	64	11			0.75-1.94
Parents living status	Lived together	262	90.3	498	85.8	0.061		1.54
	Not lived together	28	9.7	82	14.2			0.78-1.99

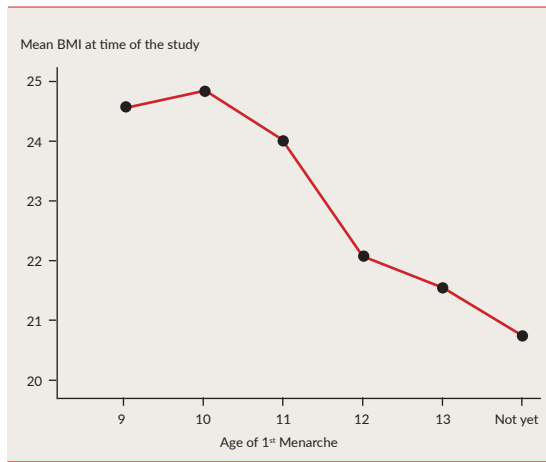


Figure 1 | The relation between means of BMI at time of study and age of 1st menarche among girls.

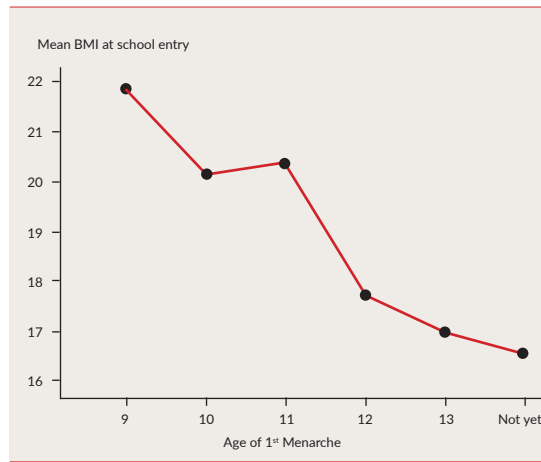


Figure 2 | The relation between means of BMI at school entry time and age of 1st menarche among girls.

students' height at school entry was not significantly associated with early menarche, contrary to the current height of girls and height difference, which showed a highly significant association ($p = 0.001$, $OR = 1.82$).

Girls with a father who completed secondary school and above have a 1.67 times chance of having early menarche than girls whose fathers have only a primary school level of education, with an OR of 0.66 and a p -value of 0.0001. Similarly, girls whose mothers had only primary educational levels had menarche later than those whose mothers had secondary or university educational levels, with an OR of 0.82 and 0.44, respectively and a p -value of 0.0001. Girls whose mother or sister did not have a history of early menarche were protected from early menarche, with an OR of 0.14 and 0.48) respectively. We found that the size of the families, the absence of the father due to death or otherwise, and broken families due to parental divorce or separation have no

statistically significant association with early menarche, with p -values of 0.219, 0.433 and 0.061, respectively. See **Table 4**

Table 5 shows the parameters showed a statistically significant association with early menarche compared to the control group measured by binary logistic regression.

DISCUSSION

Changes in puberty timing have implications for the need for care of children and the risk of later adult disease. The onset of menstruation (menarche) is one of the most visible signs that a girl is entering puberty. [20] Female Children who get early puberty are at risk for accelerated skeletal maturation, short adult height, psychosocial difficulties, and alarm for the development of reproductive tract cancers like breast cancer later in life.

Those who menstruate earlier, at age 11

Table 5 | The binary logistic regression of different factors on age of menarche.

Parameters	OR	P value	95% C.I. for	
			Lower	Upper
Obesity at school entry	2.493	0.000	3.93	11.51
Obesity at study time	1.906	0.000	3.96	37.03
Height status at time of study	0.001	0.900	0.988	1.014
Positive family history of early menarche	1.300	0.000	2.21	6.11
Father having a university certificate	0.633	0.035	0.53	0.29
Mother having a university certificate	0.861	0.006	0.62	0.29
Constant	5.6359	0.000		

years, also suffer from a poorer attitude toward menstruation, more likely to report severe menstrual symptoms, have a poorer preparation for menarche, have a poor body image, and may have low self-esteem.^[21]

It is essential to find out the mechanisms of the timing of puberty and the reasons for its alterations and provide tools for improved children's health risk assessment.^[22] Our study highlights the need for more awareness about early menarche and the need to reinforce prevention around early puberty.

Studies and surveys done in Baghdad, Tikrit, Basra, and the neighbouring countries^[8,9,23] showed an association between age at menarche and other factors. These studies had descriptive cross-sectional designs, so we chose a more analytical study like case-control to provide a qualitative and quantitative measurement of the menarche and factors affecting its onset.

This study's main objective was to determine the association between the onset of menarche and BMI and different social variables. We found that the prevalence of obesity was 6.4% and that overweight and obese girls at school entry were associated with early menarche compared to their peers with normal BMI. Similarly, we also found a significant association between obese and overweight girls at the time of study and their history of early menarche compared with girls who had normal BMI. It has been stated that children's obesity may contribute to the declining age of menarche.^[24] A study conducted in Virginia, USA, in 2001 reported that childhood obesity is an important contributing factor to the earlier onset of puberty in girls.^[25]

Several explanations for the association between the age of menarche and obesity are proposed, though the specific mechanisms remain unclear. One of the possible explanations is that higher subcutaneous fat, increased fat deposition in peripheral adipose tissues or higher level of BMI at pre-pubertal ages (5-9 years) all lead to an increase in the production and availability of estrogen through various mechanisms, which predispose to early me-

narche.^[26, 1, 27]

The critical weight hypothesis suggested that weight is influenced by a certain level of leptin, which is a protein hormone that regulates body weight, metabolism and reproductive function. A critical blood leptin level is necessary to trigger the reproductive ability of young women. At least a fat body composition of 22% is needed to exert a regulatory effect on triggering menstrual cycling in women through the synthesis of leptin.^[28, 29]

Many studies, Abdulla in Tikrit,^[9] Almulla in Basra,^[23] and Al-Awadhi in Kuwait,^[30] had shown that age of 1st menarche was inversely and significantly associated with odds of overweight and obesity in girls, after adjusting for potential confounders. In contrast, Shaik's study in Riyadh/ Saudi Arabia showed no significant correlation between BMI and age at menarche ($P>0.05$), but the researcher attributed this contradictory result to the small size of the sample and the design of his study that was cross-section.^[31]

Although the girls with early menarche were taller than girls in the control group, the association between age at menarche and height of the girls was statistically non-significant. The explanation may be compatible with Ellison, who related menarcheal age to height rather than weight, suggesting that skeletal maturation is more important than body fat accumulation for menarche.^[32] Another explanation is related to the hypothesis that menarche usually follows approximately one year after the growth spur due to the effect of the growth hormone, which seems to increase during puberty.^[33] Our results agreed with Chang from Taiwan^[34] and Onland-Moret (European Prospective Investigation into Cancer and Nutrition),^[35] who found that early menarche causes premature closure of the epiphyseal plates and thus, women with earlier menarche became taller at puberty period but shorter adult height in future when compared with women who have menarche at later age.

In our study, we found that girls of parents with high education levels get menarche earlier than girls of parents with primary school

educational levels. This may be due to more attention paid by educated parents to their children, leading them to consume more unhealthy food with less physical activity, a lifestyle that affects the general health of their girl, particularly reproductive health, triggering early menarche.^[33] Almulla Study in Basra^[23] and a study from Saudi Arabia^[31] found similar results.

Age of menarche is a strongly heritable trait; girl who do not have a history of early menarche among her mother or sisters were less likely to have early menarche. Several studies demonstrated the possible genetic role in the age of menarche, although the specific genetic determinants are unknown. Factors that regulate early maturation, including genetic and epigenetic influences, affect the timing of puberty. Mothers with earlier age menarche may indicate a trans-generational influence toward a faster maturation of girls childhood growth, which is transmitted to her offspring predicting early maturation.^[36] These results agreed with those of studies conducted by Abdulla in Tikrit,^[9] Ong in the UK,^[37] and Mee-Hwa Leel in Korea.^[38] They stated that adolescent girls whose mothers had previously experienced early menarche were more likely to experience menarche earlier.

Absence of a father (due to death or otherwise), migration due to violence, and other stressful conditions like parental divorce or separation have shown a non-significant association with early menarche of their daughters, the results disagree with that of Abdulla in Tikrit,^[9] Tither in the USA,^[39] and Ong in the UK.^[37]

CONCLUSION

Obesity and overweight at primary school entry or the age of 12-13 years were significantly associated with early menarche among intermediate school girls. Girls from both groups have the same height at entry school. However, early menarche girls showed a significant difference in height at intermediate school age. Girls with a positive family history of early menarche and higher educational levels of parents were more prone to have early

menarche.

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Abbreviations list: Body Mass Index (BMI), Confidence Interval (CI), Odds Ratio (OR), Statistical Package for Social Sciences (SPSS), United State of America (USA).

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