Correlates of Age at Menarche Among Sixth Grade Students in Wisconsin

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ABSTRACT
We conducted a cross-sectional, school-based survey of sixth-grade girls living in the Reedsburg, Wis area school district to explore factors associated with age at menarche. Data collection included parent and student questionnaires for demographic, menstrual, physical activity, and nutritional information. School nurses conducted physical examinations to provide anthropometric measurements. Salivary samples were obtained for laboratory analysis of estradiol, estrone, estriol, and progesterone levels. Students (n=59) were an average of 11.9 years of age (range: 10-13). Nineteen students (32%) reported menarche, with an average of 11.4 years of age (range: 8-12). Cycle length of the menstruating students averaged 32.0 days (range: 25-46 days). Students’ age at menarche was positively correlated with their mothers’ age at menarche (r=0.53, P=0.02). Total caloric intake, macronutrients, hormone levels, birthweight, and family size were not associated with menstrual status. We observed an inverse association between increasing weight and earlier age at menarche (P=0.03). Students past menarche watched more television (P=0.03) and participated in fewer hours of sporting activity (P=0.08) than students who had not yet reached menarche. These preliminary data suggest that further investigation of the determinants of menarche is both feasible and warranted.

INTRODUCTION
Within the scientific community, it is widely accepted that nutritional status, physical activity, and body stature are important predictors of age at menarche.1-7 These relationships are often illustrated through ecological models of global variation in age at menarche paralleled by international and racial variation in diet and nutritional status.8,9 Age at menarche serves as both an indicator of ovarian function onset and a predictor of ovulatory frequency.10 Ovarian hormones (e.g. estradiol, progesterone) have a significant impact on endogenous hormone profiles during adolescence. A relatively early or late age at menarche can be used, in part, to predict future disease risk. For example, each 1-year delay in the age at menarche is associated with a 5% decreased risk of breast cancer.11

While girls in developing countries may experience first menses at an average of 15 or 16 years of age, in the United States girls reach menarche much earlier—on average at 12.2 years for African Americans and 12.8 years for whites.9,12,13 Over the last century, a downward trend in the average age at menarche has been reported in Europe and North America.8,14 In the United States, the average age at menarche has declined markedly, a fact which may be contributing to the gradual increase in breast cancer incidence over the last several decades.14

Limited data have suggested that increased participation in sports and leisure activities is associated with later onset of menarche, while increased time without physical activity, such as time spent watching television, is associated with accelerated menarche.3,4,15 In our study, we conducted a cross-sectional survey of sixth-grade girls living in Wisconsin to explore factors associated with age at menarche.

METHODS
Student Identification and Contact
Eligibility criteria were met by all sixth-grade female students in the Reedsburg area school district of southern Wisconsin (n=101). In accordance with the institutionally-approved protocol, a letter and questionnaire were mailed to the parents of all female sixth-grade students enrolled in the school district in January.
In February 1999, investigators conducted classroom-based student surveys and brief physical examinations during school hours.

Data Collection
The parent questionnaires included questions on the mother's age at menarche and demographic information about the parents and their children (n=62 completed parent questionnaires). The student questionnaires completed in the classrooms included the Youth/Adolescent Questionnaire (a 152-item food frequency questionnaire) (n=57), and a health survey covering physical activity and menstrual status (n=59).

School nurses conducted brief physical examinations measuring height, weight, elbow width, and waist, hip, and arm circumferences according to standard protocol. Height without shoes was measured to the nearest millimeter using a stadiometer (Accustat, Genentech). Students were weighed wearing indoor clothing without shoes to the nearest 0.5 pound (Healthometer Model 134; accuracy to 300 lbs x 1/4 lb). Waist at the smallest circumference at midline, hip at the widest area between the waist and thigh, and right arm circumference at midpoint between the acromion and the tip of the olecranon were measured to the nearest millimeter using a fiberglass tape measure so that the skin was continuous along the tape but not compressed. As a measure of frame size, the left elbow width was measured (the distance between the epicondyles of the humerus) to the nearest millimeter (Lafayette Small Anthropometer Model 01291).

Laboratory analysis for estradiol, estrone, estriol, and progesterone were measured by immunoassay of saliva samples. Saliva samples were returned through the mail using kits provided by the investigators. Girls who had reached menarche were asked to provide first-morning saliva between the 20th and 23rd day (luteal phase) of their cycles. Saliva samples were returned to study staff by priority mail, frozen, then forwarded in 1 batch to Aeron Clinical Laboratory (San Leandro, CA) for hormone analysis (n=38). Students also returned by mail 3-month calendars recording any menstrual cycling (n=47).

Statistical Analysis
Characteristics according to menstrual status were computed using analysis of variance (SAS proc glm) and were adjusted for age. Selected macronutrients and hormone measurements were log-transformed in the statistical models and back-transformed for tabular presentation.

RESULTS
The students, all sixth-graders, were an average of 11.9 years of age (range: 10-13). Nineteen students (32%) reported menarche, with an average of 11.4 years of age (range: 8-12). Cycle length of the menstruating students averaged 32.0 days (range: 25-46 days).

<p>| Table 1. Means (and Standard Deviations) of Characteristics of Female Sixth-Graders According to Menstrual Status |
|-----------------|-----------------|-----------------|-----------|</p>
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Menstruating n=19</th>
<th>Not Menstruating n=40</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>12.0 (0.1)</td>
<td>11.8 (0.1)</td>
<td>0.06</td>
</tr>
<tr>
<td>Mother's age at menarche</td>
<td>12.0 (0.4)</td>
<td>12.8 (0.3)</td>
<td>0.16</td>
</tr>
<tr>
<td>Number of siblings</td>
<td>1.7 (0.3)</td>
<td>1.8 (0.2)</td>
<td>0.82</td>
</tr>
<tr>
<td>Physical activity</td>
<td>13.2 (1.2)</td>
<td>9.9 (0.8)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hours of television watched per week</td>
<td>2.0 (1.0)</td>
<td>4.2 (0.7)</td>
<td>0.08</td>
</tr>
<tr>
<td>Body Size</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birthweight (kg)</td>
<td>3.4 (0.1)</td>
<td>3.6 (0.1)</td>
<td>0.17</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>61.8 (4.3)</td>
<td>50.1 (3.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>157.6 (3.9)</td>
<td>150.8 (2.8)</td>
<td>0.17</td>
</tr>
<tr>
<td>Arm circumference (cm)</td>
<td>27.2 (1.2)</td>
<td>23.9 (0.8)</td>
<td>0.03</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.81 (0.01)</td>
<td>0.82 (0.01)</td>
<td>0.59</td>
</tr>
<tr>
<td>Elbow width (cm)</td>
<td>6.38 (0.13)</td>
<td>6.17 (0.09)</td>
<td>0.2</td>
</tr>
<tr>
<td>Dietary Characteristics†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>1732 (146)</td>
<td>1722 (102)</td>
<td>0.95</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>57.3 (5.3)</td>
<td>53.9 (3.7)</td>
<td>0.67</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>27.6 (3.1)</td>
<td>28.5 (2.2)</td>
<td>0.83</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>229.3 (21.4)</td>
<td>223.4 (15.0)</td>
<td>0.83</td>
</tr>
<tr>
<td>Fiber (g)</td>
<td>11.5 (1.6)</td>
<td>12.8 (1.1)</td>
<td>0.44</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>373.2 (63.8)</td>
<td>442.3 (44.6)</td>
<td>0.52</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>11.6 (1.4)</td>
<td>12.3 (1.0)</td>
<td>0.7</td>
</tr>
<tr>
<td>Hormone Levels‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estradiol (pg/ml)</td>
<td>1.67 (0.34)</td>
<td>1.35 (0.21)</td>
<td>0.31</td>
</tr>
<tr>
<td>Estrone (pg/ml)</td>
<td>2.38 (0.30)</td>
<td>1.95 (0.19)</td>
<td>0.18</td>
</tr>
<tr>
<td>Estriol (pg/ml)</td>
<td>7.46 (0.89)</td>
<td>6.88 (0.65)</td>
<td>0.6</td>
</tr>
<tr>
<td>Progesterone (ng/ml)</td>
<td>0.03 (0.01)</td>
<td>0.03 (0.01)</td>
<td>0.64</td>
</tr>
</tbody>
</table>

*P-values from analysis of variance models comparing least-squares means adjusted for age.
†Sufficient dietary information available for 19 menstruating students and 38 students not yet menstruating.
‡Hormone levels measured for 11 menstruating students and 27 students not yet menstruating.

1999. The letter, mailed by school officials, assured the parents of the awareness and consent of the school district and the support of the local medical community regarding the study. Parents were asked to return the completed questionnaire to study personnel through the mail. Returned and signed questionnaires constituted informed consent by the parents for the investigators to approach the students for participation in the study. The parents of 62 out of 101 female students returned signed questionnaires and granted permission to enroll their daughters in the classroom-based study. In February 1999, investigators conducted classroom-based student surveys and brief physical examinations during school hours.
Overall, the mean age at menarche among the mothers of the students was 12.5 years (range: 8-17). Age at menarche of the students was positively correlated with age at menarche of their mothers \((r=0.53, P=0.02)\). Students past menarche, on average, had mothers with earlier menarche relative to students who had not yet reached menarche (12.0 versus 12.8 years of age, \(P=0.16\); Table 1). Family size, as measured by number of siblings, was not associated with menstrual status \((P=0.82)\).

Students past menarche watched more television (13.2 versus 9.9 hrs/wk, \(P=0.03\); Figure 1) and participated in fewer hours of sporting activity (2 versus 4 hrs/wk, \(P=0.08\); Table 1) than students who had not yet reached menarche.

Students past menarche were on average heavier (61.8 versus 50.1 kg, \(P=0.03\)) and had greater arm circumferences (27.2 versus 23.9 cm, \(P=0.03\)) but not greater waist-to-hip ratios (0.81 versus 0.82, \(P=0.59\)) than students who had not yet begun menstruation. Birthweight of the students was not associated with their menstrual status \((P=0.17)\).

Dietary variables, including total calories \((P=0.95)\) and intake of protein \((P=0.67)\) or fat \((P=0.83)\), were not strongly associated with menstrual status.

Finally, estradiol, estriol, and progesterone were not strongly associated with menstrual status, although estrone levels were slightly greater in students who were menstruating (2.38 versus 1.95 pg/ml, \(P=0.18\)).

**DISCUSSION**

Our exploratory findings are in agreement with other studies in observing that greater body weight is associated with a greater likelihood of menstruation.\(^1\)\(^-\)\(^2\),\(^7\),\(^22\)\()-\(^25\) Although greater weight and body mass at ages 9-15 clearly predict earlier onset of menstruation, the role of weight at birth in predicting age at menarche is unclear.\(^7\),\(^22\)

This pilot study is consistent with previous work that has reported null associations between specific dietary foods, macro- or micronutrients, and the onset of menstruation.\(^4\),\(^7\),\(^25\),\(^26\) However, some investigators have reported direct associations between age at menarche and higher fat intake,\(^7\) animal protein consumption,\(^27\) vitamin A intake,\(^22\) and intake of seeds and nuts.\(^7\) Maclure et al\(^7\) suggest that nutrition affects timing of menarche only through its influence on accumulation of adipose tissue. Several studies have shown an association between age at menarche and height, which is an indicator of early-life nutritional sufficiency.\(^1\),\(^7\),\(^22\),\(^25\),\(^27\) In contrast to the strength of associations between height and menarche detected in studies of women born in the 1930s and 1940s,\(^1\),\(^27\) this study and other more recent studies\(^7\) have found relatively weaker associations between these factors, perhaps reflecting that most girls who live in developed countries are no longer developmentally restricted by food limitations.

Among students who reported menstruation, age at menarche was positively correlated with mother’s age at menarche \((r=0.53, P=0.02)\). Cohort, case-control, and cross-sectional studies have all previously reported associations with the age at menarche of mothers and sisters.\(^4\),\(^22\),\(^25\) It is unclear whether this association reflects shared genetic or environmental influences. Family size and number of siblings may additionally influence age at menarche as a marker of socioeconomic status, length of maternal birth intervals, or food competition.\(^28\)

The onset of menstruation is not simply a function of reaching a critical body weight.\(^29\) Several factors not discussed above have also been described as playing a role in menarche, such as season of the year,\(^3\) race/ethnicity,\(^13\) and psychosocial factors.\(^23\),\(^24\)

Our preliminary data suggest that physical activity is an important correlate of menarche in young girls. In our sample, students past menarche reported more hours of television-watching (13.2 versus 9.9 hrs/wk, \(P=0.03\)) and fewer hours of sporting activity (2 versus 4 hrs/wk, \(P=0.08\)) than students who had not yet reached menarche. Although limited, data from previous studies have suggested that increased participation in sports activities is associated with delayed menarche, while increased physical inactivity, such as watching television, is associated with earlier menarche.\(^3\),\(^15\) Greater time in sedentary activities, such as watching television, is associated with increasing body mass and body fat in children.\(^31\)-\(^34\)

In addition to its effects on the age at menarche, physical activity is also associated with anovular menstrual cycles.\(^35\) A greater cumulative number of ovulatory menstrual cycles increases breast cancer risk. Reducing the number of
Delayed menarche may be beneficial in reducing disease risk. For example, breast cancer risk may be reduced by limiting the time during which breast terminal end buds are not fully differentiated—a particularly susceptible time when cell proliferation may be increased and cancer induction may occur in the presence of environmental carcinogens. However, delayed menarche may also have unknown detrimental effects on other health outcomes, such as bone fracture and bone mineral density.

Several limitations should be considered when interpreting findings from this study. The cross-sectional study design does not allow us to determine the temporal sequence of events surrounding age at menarche. As a result, our data is insufficient to provide evidence of a causal relationship between inactivity and age at menarche. In addition, comparisons were limited by our small sample size, low variation in the ages of the students, and the high proportion of students who had not yet menstruated.

By asking students to complete a survey of recent diet, physical activity, television watching, and onset of menarche, we believe that students were able to provide accurate responses. However, as with all epidemiologic studies that use self-reported information, the potential for exposure misclassification should be addressed. We believe misclassification was unlikely to occur differentially by menstrual status. While non-differential misclassification would not result in substantial bias in the direction of detected associations, the strength of our estimated correlations may have been attenuated. Finally, although we are confident that our study’s findings are internally valid, our results may not be generalizable to other student populations. Despite these limitations, this study successfully accomplished its primary methodological aim: to quickly and efficiently provide pilot data for prospective studies of menarche.

In summary, this study supports the associations between increasing body weight, physical inactivity, and earlier onset of menstruation. Within our study, dietary factors were not clearly associated with age at menarche. Participation in physical activity and fewer hours spent watching television may be important predictors of delayed menarche.

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REFERENCES
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