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RESEARCH ARTICLE

The Relationship Between Short Chain Fatty Acids and Menarche in Elementary School Students in Padang City

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Abstract

Introduction*: Early menarche is associated with long-term health problems. Currently, adolescent girls are increasingly experience the change of menarche age. Short chain fatty acids (SCFA) are known to play a role in the early release of GnRH which induces an earlier onset of menarche. However, so far there have been no human studies assessing SCFA levels in individuals with early menarche.*

Method*: This is a case-control study in elementary school students in Padang which conducted from July 2024 to November 2024. The sample was all elementary school students in Padang who met the inclusion and exclusion criteria. The data collected were demographic data and SCFA levels measured in faecal samples using the ELISA method. Bivariate analysis was performed using the unpaired T-test.*

Result*: In this study, there were 25 students with early menarche and 25 normal students. Students with early menarche experienced the earliest age of menarche in 9 years old, 56% had excessive BMI, 20% had mother history of early menarche, 20% were born prematurely, 52% had high-fat diet, 100% lived with their parents and had no history of pornography exposure. This study found the differences in fecal SCFA levels based on age of menarche with the mean SCFA levels found to be higher in the early menarche group compared to normal menarche (39.09 ± 6.64 vs 26.91±5.01 µmol/gram; p=0.000)*

Conclusion*: This study found the differences in fecal SCFA levels based on age of menarche*

Keywords: *SCFA, early menarche*

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INTRODUCTION

Puberty is a period of transition from childhood to adulthood involving sexual maturation. Menarche, the first menstrual event, is a critical marker of female reproductive capacity. Early menarche is generally defined as menarche before the age of 12. Globally, the age of menarche has shown a rapid and continuous decline. In Indonesia, the onset of menstruation is occurring faster in the current generation, a trend believed to be linked to unhealthy lifestyles and obesity.[1,2]

Early menarche is associated with significant physical and psychosocial problems. These include early epiphyseal plate fusion, resulting in shorter adult stature, as well as higher rates of anxiety, depression, and substance use. Medically, it is linked to increased risks of type 2 diabetes, obesity, dysmenorrhea, and preeclampsia. Studies in Indonesia have consistently found a link between excess nutritional status (overweight and obesity) and the incidence of early menarche.[3–6]

This excess weight status is associated with inflammatory markers, gut microbiota composition, and Short-chain fatty acid (SCFA) concentrations. SCFAs are formed from the fermentation of indigestible dietary fibers by gut microbes and are known to regulate multiple organ systems, including the hypothalamic-pituitary-gonad (HPG) axis.[7,8]

A potential mechanism suggests that high SCFA concentrations induce leptin gene expression, which in turn activates the HPG axis and causes an earlier onset of menarche. Leptin, an adipocyte-derived peptide, is known to be critical for menarche. However, this link remains controversial, as other studies suggest leptin levels are more influenced by total body fat (waist circumference) rather than SCFA concentrations directly.[9]

While some research indicates a potential role for SCFA in activating the HPG axis, the scientific evidence remains inconsistent.[7,9] As the prevalence of early menarche continues to rise, including in Indonesia, there is a need to evaluate the mechanisms that are risk factors. To date, no studies have specifically assessed the relationship between SCFA and the age of menarche in Padang. Therefore, this study aimed to determine the relationship between Short Chain Fatty Acid levels and menarche in elementary school students in Padang City.

METHODS

This analytical study utilized a case-control design to compare short-chain fatty acid (SCFA) levels in female elementary school students in Padang City who experienced early menarche with those who did not. The research was conducted from June to November 2024.

The study population consisted of female students at State Elementary Schools in Padang. Samples were obtained using consecutive sampling from five schools: SDN 01 Bungo Pasang, SDN 11 Lubuk Buaya, SDN 10 Sungai Sapih, SDN 21 Lubuh Lintah, and SDN 03 Alai. The case group included students aged ≤12 years who had already experienced menarche (early menarche). The control group consisted of students aged 12 years who had not yet experienced menarche. Exclusion criteria for both groups included ongoing hormonal therapy, comorbidities identified through anamnesis (such as thyroid disease, pituitary tumor, or diabetes), use of

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antibiotics or probiotics in the past three months, and current gastrointestinal symptoms such as diarrhea or gastritis. Based on the sample size calculation, a minimum of 24 participants per group was required, for a total of 48 samples.

Data collection included a questionnaire to obtain basic data (age, weight, height) and menstrual history. The dependent variable, early menarche, was defined as the first menstruation occurring before age 12, determined through interview. The independent variable was the total fecal SCFA level.

Fecal samples (2–5 g) were collected in sterile tubes and transported in a cool box with ice gel to the Biomedical Laboratory, Faculty of Medicine, Andalas University, for analysis. SCFA levels (acetate, propionate, and butyrate) were measured using an ELISA kit. Fecal samples were homogenized, centrifuged, and the supernatant was analyzed according to the ELISA protocol. The procedure involved adding standards and samples to a pre-coated plate, followed by incubation, washing, addition of HRP-conjugate, chromogen solutions (A and B), and a stop solution. Optical density (OD) was read at 450 nm, and SCFA concentration (µmol/gram) was calculated from the standard curve.

Data were processed using SPSS. Univariate analysis was used to describe data distribution, and the Shapiro–Wilk test was applied to assess normality (as $N < 50$). Since the data were normally distributed, the Independent T-test was used to compare SCFA levels between the two groups. A p-value < 0.05 was considered statistically significant.

RESULT AND DISCUSSION

This study included 50 participants, divided into 25 students in the early menarche group and 25 students in the normal menarche (control) group.

Characteristics of Subjects

The mean age of menarche in the early menarche group was 10.24 ± 0.66 years, with a range of 9 to 11 years. This finding is consistent with other studies in Indonesia showing a declining trend in menarcheal age, with 9 years being the youngest reported.[10]

A significant finding was the high prevalence of excess nutritional status in the early menarche group: 60% were overweight and 24% were obese, totaling 84% with an excess BMI. This strongly supports previous research linking overweight–obese status in adolescents to early menarche, a relationship likely mediated by increased leptin from adipose tissue that activates the hypothalamic–pituitary–gonadal (HPG) axis.[7,11,12]

Other characteristics of the early menarche group included a family history (mother or sibling) of early menarche (20%), preterm birth (8%), and parents with income below the regional minimum wage (20%). All participants in both groups lived with their parents. The 20% family history link supports a genetic component, such as estrogen receptor polymorphisms, in determining menarcheal age.[13,14]

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SCFA Levels and Relationship with Menarche

The mean short-chain fatty acid (SCFA) level in the normal menarche (control) group was 26.91 ± 5.01 µmol/gram. This is consistent with the normal range for total SCFA in healthy individuals reported in other studies (approximately 19–32 µmol/g).[13,14]

In contrast, the mean SCFA level in the early menarche group was 39.09 ± 6.64 µmol/gram. This level is notably higher than that in the control group and exceeds the normal range reported in previous literature.[13]

Bivariate analysis confirmed that this difference was statistically significant (p = 0.000). Thus, SCFA levels were significantly higher in the early menarche group compared to the normal menarche group. This finding appears to contradict results from animal models. In rodent studies, high-fat diets induce early puberty but are associated with decreased SCFA production. Furthermore, SCFA supplementation in these animal models can reverse high-fat–diet–induced early puberty, suggesting a protective role.[15]

However, the results of this study are consistent with emerging human research, particularly from Asia, which highlights important inconsistencies between animal and human models. Studies on children with idiopathic central precocious puberty have reported an enrichment of SCFA-producing bacteria (such as *Ruminococcus*, *Roseburia*, and *Coprococcus*), as well as a positive correlation between *Bacteroides* and FSH levels.[16]

Several mechanisms may explain why higher SCFA levels are associated with early menarche in humans:

1. Energy Surplus Signal: SCFAs are a significant energy source. High levels may be interpreted by the body as a signal of energy surplus, which is a known trigger for activating the HPG axis and initiating menarche.[17,18]
2. Dietary Differences: The high-fat diets used in animal models differ from human diets. The diet in Padang, which may be rich in refined carbohydrates, could selectively enrich different butyrogenic (SCFA-producing) taxa, leading to different metabolic outcomes.[19]
3. Hormonal Interaction: SCFAs, particularly butyrate, can stimulate leptin expression—the critical permissive hormone for GnRH activation. High SCFA levels may therefore amplify the leptin signal from adipose tissue to the hypothalamus, accelerating HPG maturation.[17,20]
4. Gut–Brain Axis: SCFAs can cross the blood–brain barrier and directly modulate hypothalamic function, including neurotransmitters such as GABA and serotonin that influence GnRH and kisspeptin neurons, which trigger puberty.[21,22]

This study suggests that SCFAs should not be viewed as a simple protective factor, but rather as a complex biomarker reflecting a specific metabolic and microbial state (likely diet-driven) that promotes earlier pubertal timing. This aligns with previous findings indicating that enrichment of SCFA-producing bacteria may enhance leptin expression through elevated SCFA concentrations, leading to HPG axis activation and early menarche.[17,23]

Strengths and Limitations

This is the first study in Padang to assess the relationship between fecal SCFA levels and early menarche in humans, providing an important reference for future biological research on puberty. Limitations include reliance on anamnesis for exclusion criteria without diagnostic confirmation,

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which introduces potential classification bias. Moreover, the study did not measure intermediate molecules (such as leptin) to confirm the proposed mechanism, nor did it assess participants' dietary patterns, which can influence microbiota composition and SCFA levels.

CONCLUSION

Based on this research, students in Padang experiencing early menarche were predominantly characterized by an excess nutritional status (high BMI). Metabolically, the early menarche group had significantly higher levels of fecal Short Chain Fatty Acids (SCFA) compared to the normal menarche group. This statistically significant finding indicates a strong association between these gut-derived metabolites and the timing of menarche. This study provides an initial foundation for considering SCFA as a potential biological biomarker for pubertal maturation, particularly in the context of nutritional status and diet in an urban Indonesian population.

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