

Relationship between early pubertal maturation and asthma: The role of adiposity rebound in early childhood

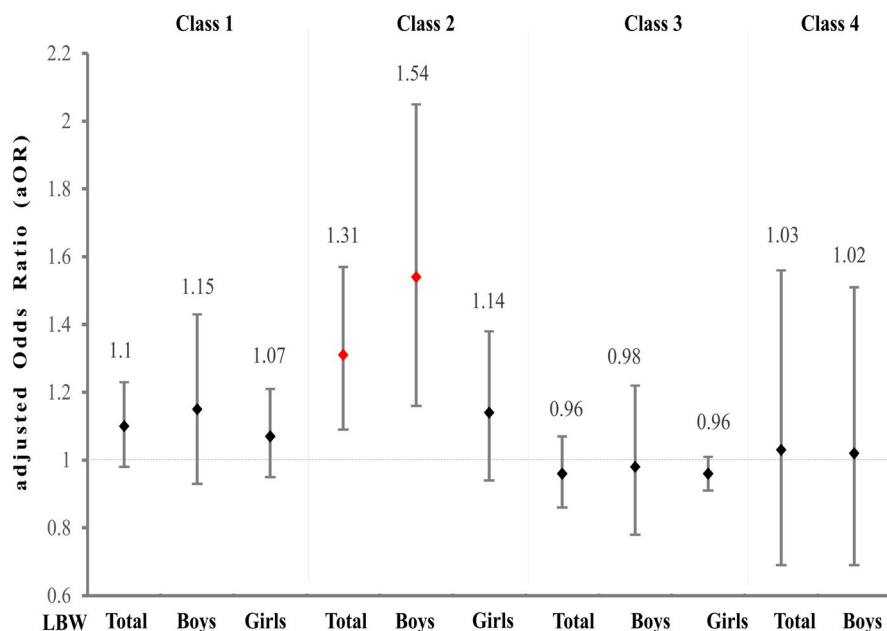
We thank Dr Ichikawa et al for their insightful remarks on our article,¹ recently published in *Allergy*, regarding early pubertal maturation and the risk of asthma. In our article, we reported that Mendelian randomization analysis revealed early pubertal maturation led to active asthma in 2991 children aged 11–12 years participating in the Taiwan Children Health Study (TCHS). Moreover, early pubertal maturation considerably increased the risk of incident asthma outcomes at 12 and 17 years in both sexes by conducting longitudinal study analysis. In the correspondence letter to the Editor, Dr Ichikawa et al proposed two possible pathways of early adiposity rebound (AR) to asthma²: (a) early AR → obesity → early pubertal maturation → asthma and (b) early AR → storage of fat but no obesity → early pubertal maturation → asthma. In this reply letter, although adiposity data during the early childhood (from 1 to 5 years of age) were not collected, we defined AR using birth weight and body mass index (BMI) trajectory patterns (BMI during 6–11 years of age) from the TCHS to evaluate the hypothesis proposed by Dr Ichikawa et al.

On the basis of a latent generalized mixture model,³ four distinct BMI trajectory patterns were identified between the ages 6 and 11 years from the data in our previous study⁴: the normal growth class (Class 1), rapid growth class (Class 2), persistently overweight class (Class 3), and declining obesity class (Class 4). The Class 1 children demonstrated BMI z-scores of nearly 0 at ages of 6–11 years. The children in Class 2 had normal BMI at 6 years of age but their

BMI z-score had increased to 1 at the age of 11 years. The Class 3 children had long-term overweight and obesity during 6–11 years of age. The children in Class 4 demonstrated a significant decline in BMI z-score from >4 to <3. Being persistently overweight (Class 3) at the ages of 6–11 years has a profound and long-term effect on incident asthma.³ Herein, the relationships between BMI trajectory classes and risk of early pubertal maturation were further investigated in children with low birth weight (LBW). Children with normal birth weight and belonging to the BMI trajectory Class 1 were used as the control group. Children who experienced AR and became obese (early AR → obesity) were originally of LBW but later became children in BMI trajectory Classes 2, 3, and 4. Those who experienced AR but did not become obese (early AR → storage of fat but no obesity) were originally of LBW but later became normal weight children in BMI trajectory Class 1. As illustrated in Figure 1, children who had LBW but later entered the rapid growth class (BMI trajectory class 2) had significantly higher risk of early pubertal maturation, especially when they were boys (OR, 1.31; 95% CI, 1.09–1.57 for all children; OR, 1.54; 95% CI, 1.16–2.05 for boys; and OR, 1.07; 95% CI, 0.95–1.21 for girls).

We concluded that children with AR had increased risk of early pubertal maturation. Our results support the hypothesis, early AR → obesity → early pubertal maturation → asthma that was proposed by Dr Ichikawa et al, and the findings are in accordance

FIGURE 1 Odds ratios of early pubertal maturation at 11–12 years for children with low birth weight, divided into four distinct BMI trajectory classes. Footnote: Class 1, normal growth; Class 2, rapid growth; Class 3, persistently overweight; Class 4, declining obesity. LBW, low birth weight; Reference group: Class 1 children with normal birth weight; No girls with LBW were observed in class 4. All models were adjusted for age, parental education, family income, birth weight, and household smoking exposure



with previous studies.⁵ Prenatal growth restriction followed by postnatal catch-up growth may be associated with early pubertal maturation. Additionally, studies have explored the effect of BMI growth in early childhood on asthma,^{6,7} and the critical period for rapid adiposity growth on asthma risk was found to be 1–4 years.⁷ Moreover, nutritional rehabilitation of infants who are small for gestational age leads to AR, coincident with increased gonadotropin secretion and eventually leading to early puberty. Our result did not support the second hypothesis: early AR → storage of fat but no obesity → early pubertal maturation → asthma. However, other studies have reported that girls with early puberty might experience AR and have excess body fat mass and central fat mass compared with matched controls, even if they were not categorized as obese children.⁸ These findings imply that physicians and caregivers should emphasize early intervention more strongly to prevent childhood adiposity.

CONFLICT OF INTEREST

The authors declare that no competing interests exist.

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Yang-Ching Chen^{1,2,3,4} 

Yungling L. Lee⁵ 

¹Department of Family Medicine, Taipei Medical University Hospital, Taipei, Taiwan

²Department of Family Medicine, School of medicine, College of medicine, Taipei Medical University, Taipei, Taiwan

³School of Nutrition and Health Sciences, College of Nutrition, Taipei Medical University, Taipei, Taiwan

⁴Graduate Institute of Metabolism and Obesity Sciences, Taipei Medical University, Taipei, Taiwan

⁵Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan

Correspondence

Yang Ching Chen, Department of Family Medicine, Taipei Medical University Hospital, Taipei Medical University, No. 252, Wu-Hsing St, Xinyi District, Taipei 11031, Taiwan.

Email: melisa26@tmu.edu.tw

Yungling Leo Lee, MD, PhD, Institute of Biomedical Sciences, Academia Sinica, 128 Academia Road, Sec. 2, Taipei 11529, Taiwan.

Email: leolee@ibms.sinica.edu.tw

ORCID

Yang-Ching Chen  <https://orcid.org/0000-0002-0682-3716>

Yungling L. Lee  <https://orcid.org/0000-0002-2234-9479>

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