



Yogurt consumption in infancy is inversely associated with atopic dermatitis and food sensitization at 5 years of age: A hospital-based birth cohort study



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ABSTRACT

Background: Several studies have suggested that habitual yogurt consumption is associated with favorable outcomes for health issues in children. However, the effects of yogurt consumption on allergic diseases and sensitization in children remain poorly understood.

Objective: This prospective birth cohort study aimed to investigate for associations between habitual yogurt consumption in infancy and development of allergic diseases/sensitization at 5 years of age.

Methods: Data were obtained from the Tokyo Children's Health, Illness and Development (T-CHILD) study. A total of 1550 children were born to the recruited women. Consumption of yogurt by children during infancy was determined by using questionnaires completed at 12 months of age. Outcome data for children were collected from the questionnaires and medical check-ups completed at 5 years of age. Possible associations between habitual yogurt consumption in infancy and allergic diseases/sensitization were analyzed by multiple logistic regression analyses.

Results: We analyzed the data for 1166 children whose parents responded at 5 years of age. Habitual yogurt consumption in infancy and atopic dermatitis at 5 years of age were significantly associated (UKWP criteria: aOR, 0.70; 95% CI, 0.51–0.97; $P=0.03$). Children with habitual yogurt consumption in infancy were less likely to be sensitized to food allergens (aOR, 0.53; 95% CI, 0.31–0.93; $P=0.03$), but no associations were seen in regard to any other allergens.

Conclusions: Our study demonstrated that habitual consumption of yogurt in infancy has the potential to prevent development of atopic dermatitis and food sensitization, but not other allergic diseases, at 5 years of age.

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1. Introduction

The increasing prevalence of allergic diseases, especially in westernized countries, is becoming a public health burden. One of the leading theories to explain the modern-day allergy epidemic was proposed by Strachan in 1989, namely, the hygiene hypothesis [1]. Drawing on the hygiene hypothesis, the apparent rise in the prevalence of allergic diseases might be due to reduced early-life

environmental exposure to microorganisms, with consequent alteration in the balance of the immune response [2].

Growing evidence supports a pivotal role for infant gut colonization in the development of the immune system [3]. A decrease in certain microbes such as lactobacilli and/or gut microbiota diversity, especially during early childhood, seems to be associated with subsequent development of allergic diseases [4]. In this context, manipulation of the intestinal microbiota by probiotic

Abbreviations: T-CHILD, Tokyo Children's Health, Illness and Development; OR, odds ratio; CI, confidence interval; ISAAC, International Studies of Asthma and Allergies in Childhood; UKWP, United Kingdom Working Party.

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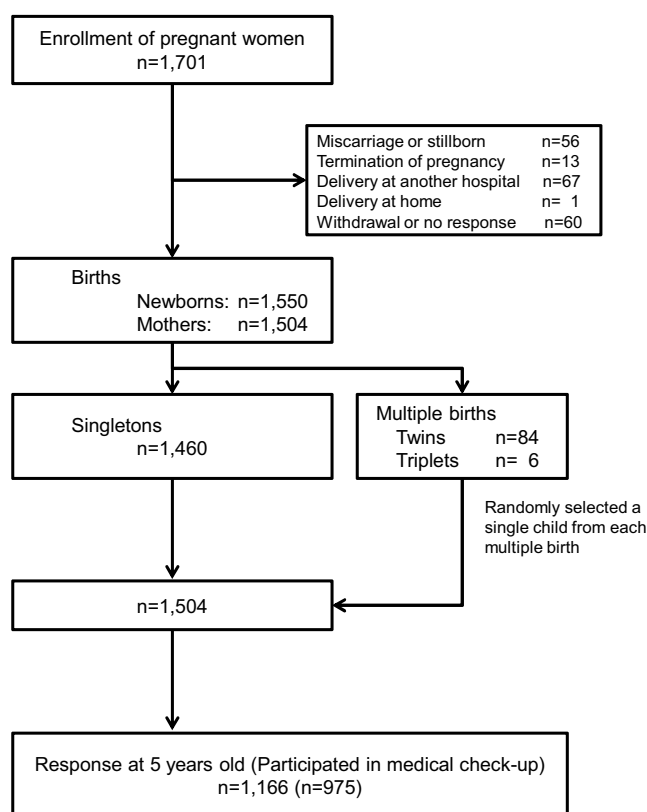


Fig. 1. Flow chart of the study population.

supplementation has been thought to be potentially beneficial in prevention of allergic diseases. Indeed, recent systematic reviews and meta-analyses of randomized controlled trials showed that probiotics used by pregnant women or breastfeeding mothers and/or given to infants at high risk of allergic diseases reduced the infants' risk of atopic dermatitis/eczema, but not other allergic diseases [5,6]. However, it is still uncertain whether these strategies would protect against allergic diseases in an unselected population (i.e., children both with and without a parental history of allergic diseases).

Yogurt, one of the best-known foods that contain probiotics, is produced by culturing dairy ingredients with lactic acid bacteria [7]. Yogurt consumption, probably through its effect on the gut microbiota, was associated with favorable outcomes for health issues in children [8]. As for allergic diseases, Roduit et al. investigated for an association between introduction of yogurt in the first year of life and the protective effect against atopic dermatitis [9]. Notably, they showed promising and intriguing results that early introduction of yogurt prevented atopic dermatitis, with statistical significance (odds ratio 0.41; 95% CI, 0.23–0.73). However, they investigated only the effect on atopic dermatitis, not on other allergic diseases or allergic sensitization. Our analysis using the data from a prospective birth cohort study aimed to investigate for associations between habitual yogurt consumption in infancy and development of allergic diseases and sensitization.

2. Materials and methods

2.1. Study design and population

The Tokyo Children's Health, Illness and Development (T-CHILD) study, also known as the "Seiiku Cohort Study", was a single-center, prospective, hospital-based birth cohort study. The

design of this study has been described in detail elsewhere [10]. Briefly, the T-CHILD study enrolled 1701 pregnant women under 16 weeks' gestation from the National Center for Child Health and Development (NCCHD), Tokyo, Japan between October 2003 and December 2005. A total of 1550 children were born to the recruited women between March 2004 and August 2006. In the case of multiple births in this study population, we randomly selected one of the children for inclusion in the analysis. For the examination at 5 years of age, 1166 mothers of children responded to the questionnaire, and 975 children participated in the medical check-up. Data with missing values were deleted when fitting to the models.

2.2. Questionnaire

Data from surveys conducted during maternal pregnancy and when children were 12 months and 5 years of age were analyzed in this study.

Consumption of dietary yogurt by the children during infancy was determined based on the reply to the following question at 12 months of age: "Over the past 12 months, how often did your child eat yogurt, lactobacillus-fermented milk or products?" The intake frequencies of yogurt were classified into three groups as a dietary habit during infancy: 1) none, 2) sometimes, and 3) every day. A response of "3) every day" was considered to be habitual yogurt consumption.

Allergic diseases were investigated using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire, which was completed by parents when their children were 5 years old [11] (Table E1). The ISAAC questionnaire was translated into Japanese and validated. Additionally, we collected the data on atopic dermatitis, which was formally diagnosed using the United Kingdom Working Party (UKWP)'s diagnostic criteria [12] at medical check-up at 5 years of age.

Variables considered to be potential confounders were as follows: parental history of allergic disease, gender, preterm birth, mode of delivery, season of birth, smoking during pregnancy and pet ownership during pregnancy. Data on those variables were obtained from questionnaires completed at 16, 23 and 34 weeks' gestation and the medical charts. Data on breast feeding, timing of solid food introduction, history of food allergy until 1 year, history of wheeze until 1 year, history of eczema until 1 year, number of previous live births and daycare during infancy were obtained from questionnaires completed at 12 months of age.

2.3. Sensitization

Serum samples were obtained from participants at 5 years of age, and aliquots were frozen and stored at -30°C until assay. Specific IgE concentrations in serum samples were determined using the molecular multiplex test ImmunoCAP[®] ISAC (Thermo Fisher Scientific, Uppsala, Sweden), [13,14]. Sensitization was defined as a positive result for any single allergen if a specific IgE level of ≥ 0.3 ISAC standardized units (ISU) was observed. The sensitizing antigens (103) are shown in Table E2 and include 40 food allergens and 53 inhalant allergens, plus 10 miscellaneous allergens.

2.4. Statistical analysis

Differences in the characteristics of children stratified as to habitual yogurt consumption in infancy were tested as categorical variables using the chi-square test. We built logistic models to estimate associations between habitual yogurt consumption in infancy and allergic diseases in children at 5 years of age. We built the models as follows: first, we fitted model 1 with all the potential

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