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Birth weight and type 1 diabetes among schoolchildren in Taiwan—A population-based case-controlled study

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Abstract

To explore the relationship between birth weight and type 1 diabetes, data from national birth registry and national surveillance of diabetes in Taiwanese schoolchildren were analyzed. From 1992 to 1997, all schoolchildren aged 6–18 years were screened for diabetes by a mass urine survey program in Taiwan Province. This cohort consisted of 1966 children with diabetes and 1780 of randomly selected subjects with normal fasting glycemia. Questionnaires were designed for telephone interviews with students' parents or physicians to classify subjects' types of diabetes. The birth history of each participant was obtained from the Taiwan's Birth Registry. After merging the data, there were 835 subjects, including 277 of type 1 diabetes and 533 of normal fasting glycemia available for the present analyses. The odds ratio (95% CI) for type 1 diabetes, after adjusting age, sex, socioeconomic status, family history of diabetes, birth order, breast-feeding, BMI, and gestational diabetes mellitus was 2.24 (1.11–4.50) for children with low birth weight (<5th percentile, i.e., ≤2600 g) when compared with the referent group of a birth weight of 3000–3542 g (equivalent to the 25–75th percentile). In conclusion, low birth weight was associated with increased risk of type 1 diabetes in Taiwanese schoolchildren.
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Keywords: Birth weight; Type 1 diabetes; National survey; Schoolchildren; Case–control studies

1. Introduction

Type 1 diabetes (T1D) is primarily caused by pancreatic β cell failure that is generally believed to be a consequence of the chronic autoimmune destruction of the β cells. Exposure to some environmental factors early in life, such as viral infections and nutritional factors are considered to be pivotal in the pathogenesis of T1D [1]. Neonatal anthropometrics has been used as

Abbreviations: T1D, Type 1 diabetes; NFG, normal fasting glycemia

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a marker of neonatal environment and fetal growth to evaluate their effects on the development of T1D. While one study conducted in Europe demonstrated that low birth weight is a protecting factor [2], another study showed that high birth weight is a risk factor of T1D [3], the others have not found any relationship between birth weight and risk of T1D [4–8]. So far, there has been no nationwide, population-based study reported for Asian populations.

In Taiwan, the incidence of T1D is estimated at around 1.5 per 100,000 children per year [9]. With the advent of a nationwide mass urine screen program for diabetes in schoolchildren in the past decade, we had recruited a cohort of 1966 subjects with diabetes [10]. In this nationwide, population-based case-controlled study, we attempted to explore the relationship between birth weight and development of T1D among schoolchildren and adolescents aged from 6 to 18 years via a national registry of birth weight (Taiwan's Birth Registry).

2. Materials and methods

From 1992 to 1997, a mass-screening program for detecting diabetes and renal disease had been conducted in Taiwan Province, including all the 21 counties and cities. All schoolchildren (about 3,000,000 for each semester) from grades 1 to 12, aged 6–18 years, underwent urine screening each semester. This program was conducted by the Chinese Foundation of Health (CFH) with the support from the Taiwan Provincial Department of Health and the approval from the Provincial Education Board of Taiwan. Routinely, a letter was sent to parents to explain the program and to invite their children to participate in the program. Each student brought home instructions and a specimen container to collect the first urine sample after waking up in the morning. The student brought the specimen to school for the study team. The provision of a urine specimen was taken as consent to participate. Over 95% of the schoolchildren participated in the survey during these years. Fasting blood samples were drawn for examination purposes only after obtaining written informed consent from parents.

With consent and assistance obtained from the parents, nearly all of the students (response rate of an average of 97%) were instructed to collect the mid-stream sample of the first morning urine. After glucosuria was confirmed in two sequential urine samples within 2 weeks, a third examination was arranged for physical examination and a fasting blood sample drawn to determine levels of glucose and cholesterol. All blood samples were transferred to the central laboratory at the CFH headquarters. Blood glucose levels were measured by an automatic analyzer (Technican RA 2000 Serum Autoanalyzer, BAYER Diagnostic, USA). For quality control, CFH participated in the College of American Pathologists quality assurance program and won a Good Performance award. According to the 1997 American Diabetes Association (ADA) recommendations, subjects were classified into three categories, i.e., diabetes mellitus (DM), impaired fasting glycemia (IFG), and normal fasting glycemia (NFG) based on fasting plasma glucose (FPG) levels. These students were referred for further diagnosis and care.

During the period of 1992–1997, a total of 1966 cases of DM were identified using the 1997 ADA's criteria. For comparison, 1780 control subjects were randomly selected from all NFG ($n = 96{,}548$) students. Those with gestational weeks smaller than 37 weeks were excluded from the analysis. All students with abnormal FPG were referred for clinical diagnosis. To obtain further information to classify diabetes, we performed telephone questionnaire interviews with the students' parents regarding current weight and height, years of parental education, age at diagnosis of diabetes, modalities of diabetes therapy (diet alone, anti-diabetic oral medicines, or insulin), interval between diagnosis (screening) and initiation of insulin treatment, and the family history of diabetes and hypertension in their first-degree relatives. We also tried to contact students' physicians if the above important information were not sure by their parents. Subjects were considered to have T1D if all of the following criteria were met: (1) FPG $\geq$ 126 mg/dl at screening; (2) had received insulin injection within 6 months after diagnosis of DM; (3) a diagnosis of T1D by their referred physicians.

The data of birth weight, parental age, parental education levels on the birth day of the children and gestational age in weeks were obtained by matching the citizenship identification numbers with Taiwan's Birth Registry, Department of Internal Affairs, Executive Yuan, Republic of China.

2.1. Statistical analyses

Descriptive data were shown in means and standard deviations (S.D.) for a continuous variable, and the *t*-test and χ^2 were used for testing the differences between T1D and NFG. Birth weight was classified into five categories, i.e., $\leq$2600, 2601–2999, 3000–3542, 3543–3999, and $\geq$4000 g, which represent for $<$5, 5–25, 25–75, 75–95, and $>$95 percentile birth weight of all term

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