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Neurodevelopment in full-term small for gestational age infants: A nationwide Japanese population-based study

Original article

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Abstract

Objective: To investigate neurological development in small for gestational age (SGA) infants, with a focus on full-term SGA infants.

Methods: We analyzed data from a large, Japanese, nationwide, population-based longitudinal survey started in 2001. We restricted the study to participants born before 42 weeks of gestation (n = 46,563). Parents were asked questions about motor and language development when the children were 2.5 years old, and about behavioral development at 5.5 years. We analyzed the relationships between SGA status and development by logistic regression. Odds ratios (ORs) and 95% confidence intervals (95% CI) were calculated for each outcome for full-term and preterm births, adjusting for potential infant- and parent-related confounding factors. We also calculated the population-attributable fractions to estimate the public impact of SGA births.

Results: SGA full-term children were more likely to demonstrate developmental delays at 2.5 years, e.g., being unable to walk alone (OR 3.0, 95% CI: 1.7, 5.3), compose a two-phrase sentence (OR 1.5, 95% CI: 1.2, 1.8), or use a spoon to eat (OR 1.5, 95% CI: 1.1, 1.9). SGA status also had some degree of negative impacts on behavioral problems at 5.5 years among term children, e.g., being unable to listen without fidgeting (OR 1.2, 95% CI: 1.1, 1.3), or remain patient (OR 1.1, 95% CI: 1.0, 1.2). The public health impacts were comparable between full-term and preterm SGA children at 2.5 years.

Conclusion: SGA is a risk factor for developmental delay, even in full-term infants, with non-negligible public health impacts. © 2016 Published by Elsevier B.V. on behalf of The Japanese Society of Child Neurology.

Keywords: Behavior; Epidemiology; Growth; Development; Small-for-gestational-age

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Abbreviations: ADHD, attention-deficit/hyperactivity disorder; AGA, appropriate for gestational age; CI, confidence interval; MHLW, Japanese Ministry of Health, Labour and Welfare; OR, odds ratio; PAF, population-attributable fraction; SGA, small for gestational age

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1. Introduction

Small for gestational age (SGA) infants are reported to be at increased risks of short stature, obesity, hypertension, insulin resistance, and neurological sequelae in later life [1]. The neurological prognoses of SGA infants have been the focus of recent attention [2]. Several previous studies demonstrated that SGA was a significant risk factor for neurodevelopmental delays among preterm infants [3-5]. However, there are more SGA full-term than preterm infants, and the neurological consequences among full-term SGA infants may represent more of a public health concern. A recent metaanalysis showed that neurological development in full-term SGA infants was poorer than in full-term appropriate for gestational age (AGA) infants [6]. However, findings from large population-based birth cohorts (tens of thousands of participants) were limited in this meta-analysis. To the best of our knowledge, only two large population-based birth cohorts have evaluated the association between birth weight or SGA status and neurological consequences in full-term infants [7.8]. However, the neurological outcome that one large cohort study evaluated was limited to gross motor development [7]. In addition, another cohort study covered the period from 1959 to 1966 [8]. Thus, an analysis of a more recent cohort on wide neurological outcomes is warranted to take into account improvements in medical and educational supports for SGA infants.

In the present study, we therefore examined neurological developmental outcomes in SGA infants using data from a Japanese nationwide survey begun in 2001, focusing on full-term SGA infants, and then estimated public health impacts of SGA births among both full-term and preterm infants.

2. Methods

2.1. Study participants

The Japanese Ministry of Health, Labour and Welfare (MHLW) has implemented a survey of newborn babies and their parents, the Longitudinal Survey of Babies in the 21st Century, annually since 2001 [9,10]. Briefly, baseline questionnaires were distributed to all families throughout the country with 6-month-old infants born between the 10th and 17th January or the 10th and 17th July, 2001. Of 53,575 mailed questionnaires, 47,015 were completed and returned (88% response rate). Follow-up questionnaires were sent to the initial respondents every year, beginning at 18 months. Birth records were also linked to each child included in this survey. Birth-record data included length, weight, gestational age, singleton, twin or other multiple births, sex, parity, and parental age.

We excluded children without information on birth weight (n = 14) and then gestational week (n = 24). SGA status of the newborns was determined using published Japanese standards for birth weight according to pregnancy duration [11,12]. The standards do not include information for newborns after 42 weeks of gestational age; therefore we also excluded children born after 42 weeks (n = 414), leaving 46,563 children for analysis. We targeted children whose data were collected in the third and sixth surveys (at 2.5 and 5.5 years, respectively). A total of 4,362 children were lost to follow-up at the third survey, leaving 42,201 children, and 8,877 children were lost to follow-up at the sixth survey, leaving 37,686 children in the analysis.

2.2. SGA status

According to the International Classification of Diseases-10, SGA is defined as both birth weight and birth height below the 10th percentile for gestational age. However, SGA has been defined simply by birth weight in many previous studies [6], because of inaccuracies in birth height measurements. We therefore classified SGA babies as those whose birth weight was < 10% of the population according to pregnancy duration, based on published Japanese standards, established by the Committee for Newborns in Japanese Pediatric Society, which provide specific birth weight percentiles [11,12] for each gestational week and day. Birth weight and gestational age data were collected from birth records.

2.3. Behavioral development outcomes

Behavioral development outcomes were assessed by survey questions about age-appropriate behavior [9,10]. The questions at 2.5 years old were: (1) Can your child walk?; (2) Can your child run?; (3) Can your child climb stairs?; (4) Can your child say words with meaning?; (5) Can your child compose two-phrase sentences?; (6) Can your child say his or her own name?; and (7) Can your child use a spoon to eat? The following questions were not included, because the behaviors were potentially heavily dependent upon parenting practices: (1) Can your child brush his/her teeth by him/herself?; (2) Does your child wear a diaper during the day?; and (3) Can your child put on clothes by him/herself? The MHLW obtained the behavioral questions from the Maternal and Child Health Handbook, which is a record of health and child development given to every pregnant mother in Japan, and in which all information from postnatal visits is recorded until the child is 6 years old. The dissemination and use of the Handbook is mandated under Japanese law and has been implemented for several decades.

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