Influence of Relative Age on Diagnosis and Treatment of Attention-Deficit Hyperactivity Disorder in Taiwanese Children

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Objective To determine the potential influence of relative age on the diagnosis and treatment of attention-deficit hyperactivity disorder (ADHD), especially in reference to an Asian country.

Study design A total of 378 881 subjects aged 4-17 years during the study period (September 1, 1997 to August 31, 2011) were enrolled in our study from the Taiwan National Health Insurance Research Database. Logistic regression analysis was used to examine the likelihood of receiving ADHD diagnosis and treatment for those who were born in August (the youngest) compared with those who were born in September (the oldest).

Results Both boys and girls born in August had a higher risk of being diagnosed with ADHD (OR 1.63, 95% CI 1.45-1.84; OR 1.71, 95% CI 1.36-2.15) and receiving ADHD medication (OR 1.76, 95% CI 1.53-2.02; OR 1.65, 95% CI 1.26-2.18) than those born in September. Sensitivity tests conducted over different periods revealed consistent findings.

Conclusions Relative age, as an indicator of neurocognitive maturity, is crucial in the risk of being diagnosed with ADHD and receiving ADHD medication among children and adolescents. Our findings emphasize the importance of considering the age of a child within a grade when diagnosing ADHD and prescribing medication for treating ADHD. *(J Pediatr 2016;172:162-7)*.

Attention-deficit hyperactivity disorder (ADHD) is the most commonly diagnosed neurodevelopmental disorder. ADHD begins in childhood and manifests as an inability to marshal and sustain attention and modulate activity level and impulsive actions.[1-3] ADHD is highly prevalent in children and adolescents worldwide and affects approximately 7% of children and adolescents with a male-to-female ratio between 3:1 and 4:1.[1-3] The prevalence of ADHD ranges widely, for example, up to 15% in US and only about 5% in European countries.[4,5] The significant variation in ADHD prevalence worldwide may indicate the debate and the concern for subjectivity in ADHD diagnosis and treatment.[4,5] The specific pathophysiology of ADHD is unclear, and its etiology seems complex. Multiple genetic and environmental factors act together to induce a spectrum of neurobiological vulnerability.[1-3]

Several studies have demonstrated the potential influence of relative age on the diagnosis and treatment of ADHD in children and adolescents, indicating that a within-grade relative maturity disadvantage may be associated with a high risk of being diagnosed with ADHD and receiving ADHD medication.[6-9] Because of the cut-off birthdates for entry to school, children within the same grade may be almost 1 year apart in age; in other words, the youngest students with birthdates just before the cut-off date are much younger and less mature than their classmates born at other times of the year, particularly those born in the first month of the academic year.[6-9] Morrow et al[7] reported that because the annual cut-off birthdate for entry to school in British Columbia, Canada, is December 31, both boys and girls born in December exhibited a higher risk of receiving ADHD diagnosis (relative risk [RR]: 1.30, 95% CI 1.23-1.37; RR 1.70, 95% CI 1.53-1.88) and medication (RR 1.41, 95% CI 1.33-1.50; RR 1.77, 95% CI 1.57-2.00) than those born in January. A systematic review study conducted by Elder et al[10] also suggested that the youngest children within a grade are more likely to be diagnosed with ADHD than the oldest children, regardless of the cut-off birthdates (September 1 or December 1) for entry to school. However, a Danish nationwide study failed to validate the potential influence of relative age on the likelihood of receiving ADHD medication.[8] Pottegard et al[8] demonstrated that in the academic years between 2006 and 2012, younger sixth graders had similar risk (prevalence proportion ratio 0.97, 95% CI 0.88-1.06) of being prescribed ADHD medication as that

ADHD	Attention-deficit hyperactivity disorder
NHIRD	National Health Insurance Research Database
NTD	New Taiwan dollar
RR	Relative risk

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for older sixth graders.[8] They further suggested that this may be due to high numbers of relatively young students being held back by 1 year in the Danish school system and generally low rates of ADHD medication use in the country. On the contrary, a few relatively young students may possibly attend the school 1 year earlier because of the arrangement by their parents in Taiwan. Most of the aforementioned studies were conducted in western countries; hence, the potential effect of relative age on the diagnosis and treatment of ADHD in Asian countries remains unclear. In addition, other limitations of these studies included the lack of adjustment for demographic factors (eg, level of urbanization) in the regression models and ADHD diagnoses based on parent- or teacher-reported questionnaires rather than psychiatrist diagnoses.

This study investigated whether the impact of relative age is exclusive to western countries, such as the US, Canada, Spain, and Sweden,[7,9,11,12] or is also present in Asian countries, such as Taiwan. We conducted a cohort study to explore the effect of relative age on the diagnosis and treatment of ADHD in a large sample of subjects aged 4-17 years by using data from the Taiwan National Health Insurance Research Database (NHIRD). The cut-off birthdate for entry to school in Taiwan is August 31, and consequently, those born in August are typically the youngest in their grades. We hypothesized that those born in August are more likely to be diagnosed with ADHD and receive a prescription for ADHD treatment than those born in September.

Methods

A total of 1 000 000 subjects, approximately 4.3% of the population of Taiwan, were randomly selected from the NHIRD for the study. The study period was from September 1, 1997 to August 31, 2011. The study cohort comprised subjects aged 4-17 years during the study period. The subjects included in the cohort were followed up until the day before their 18th birthday or the end of the study period (August 31, 2011). A diagnosis of ADHD (*International Classification of Diseases, Ninth Revision, Clinical Modification* code: 314) was given at least twice by board-certificated psychiatrists during the follow-up to ensure diagnostic validity. The analysis of prescribed medication comprised methylphenidate and atomoxetine. The level of urbanization (level 1: most urbanized region; level 5: least urbanized region) and income-related insured amount were also assessed as confounding factors in our study. The income-related insured amount was defined by the monthly income of the insured subjects or family and was divided into 3 levels: ≤15 840 new Taiwan dollar (NTD), 15 841-25 000 NTD, and >25 000 NTD.

Statistical Analyses

All the subjects in the cohort were categorized on the basis of their birth month, and the prevalence of subjects diagnosed with ADHD and receiving a prescription for ADHD medication (methylphenidate or atomoxetine) was examined each month. The annual cut-off birthdate for entry to school in Taiwan is August 31. To estimate the influence of relative age, logistic regression analyses with adjustment for demographic factors (sex, level of urbanization, and income-related insured amount) were performed to determine the OR and 95% CI for receiving an ADHD diagnosis and a prescription for medication to treat ADHD for subjects who were born in August (the youngest) compared with those who were born in September (the oldest). The Cochran-Armitage trend test was used to determine the influence of relative age on diagnosis and medication across all birth months. In addition, subanalyses stratified by year and sex were performed. In the year-stratified analysis, the data were analyzed in 1-year categories spanning September to August (ie, 1997-1998 refers to September 1, 1997 to August 31, 1998), and the risk of receiving ADHD diagnosis or medication for subjects who were born in August compared with those who were born in September was analyzed. Stratified by the age group (preschool children: <6 years, school children: 6-12 years, and adolescents: >12 years), the logistic regression analyses were also performed to investigate the OR and 95% CI for the risk of ADHD diagnosis and medication for those who were born in August compared with those who were born in September. Sensitivity tests were also performed for different periods; we analyzed cohorts of subjects born between August 25 and August 31 or between August 17 and August 31 and compared them with those born between September 1 and September 7 or between September 1 and September 15. We also analyzed cohorts of subjects born between June and August (the youngest one-fourth) and compared them with those born between September and November (the oldest one-fourth). A 2-tailed P value of <.05 was considered statistically significant. All data processing and statistical analyses were performed using SPSS v 17 software (SPSS Inc, Chicago, Illinois) and SAS v 9.1 (SAS Institute, Cary, North Carolina).

Results

A total of 378 881 subjects were included in our study. The diagnosis of ADHD took place in school children (60.3%) most frequently, followed by preschool children (22.7%), and teenagers (17.0%). The prevalence of subjects who received ADHD diagnosis or medication is summarized according to the birth month in **Table I**. The prevalence of subjects receiving ADHD diagnosis or medication increased with each birth month from September (1.8% and 1.2%) to August (2.9% and 2.1%) (**Table I**). The Cochran-Armitage trend analysis indicated a significant trend for an increasing prevalence of ADHD diagnosis and medication with the birth month. The variation in ADHD diagnosis and treatment with the birth month is presented in the **Figure**, indicating an increase in the prevalence of boys and girls receiving ADHD diagnosis or medication with the birth month.

The logistic regression analyses with adjustment for demographic factors indicated that the subjects born in August