

Development patterns of adenoids in Chinese children without sleep-disordered breathing: a retrospective magnetic resonance imaging study with consecutive age groups

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To the Editor: Sleep-disordered breathing (SDB) is a health problem affecting approximately 12% of children in China,^[1] characterized by habitual loud snoring and increased respiratory effort. Increased upper airway resistance related to enlarged adenoids has been identified as the most common cause in children with obstructive SDB, and adenoidectomy is the standard treatment for the disorder. Similar to lymphoid tissues, adenoids show a unique natural growth pattern, which incorporates both overgrowth and involution. However, the development patterns of adenoids have not been clearly elucidated. Since the adenoids are located in the nasopharynx roof, direct evaluation of their size and proportion to the upper airway area is difficult. Thus, radiological methods have been employed widely for such purposes, including traditional plain cranial radiographs, computed tomography (CT), cone-beam CT, and magnetic resonance imaging (MRI). MRI can reveal the accurate size of adenoids by differentiating them from other soft tissue structures without any ionizing radiation; therefore, it can effectively study the adenoids' developmental pattern in normal children. Previous studies have evaluated age-associated changes in adenoid size by MRI. Arens *et al*^[2] indicated that adenoids grow proportionally to the skeletal structures in children aged 1 to 11 years. Papaioannou *et al*^[3] reported that head MRI examinations demonstrated increased adenoid size during the first 7–8 years of life and then decreased gradually in children without snoring signs. Variabilities of the above-reported adenoids' development pattern exist due to the limitations associated with the small sample size. Furthermore, none of the above-mentioned studies on normal children used a strict method to exclude SDB. Additionally, for adenoid hypertrophy, the adenoid/nasopharyngeal (A/N) ratio was found to be a useful, tolerable, and confident

diagnostic method in pediatric patients, with emphasis on the correlation of the adenoid size and upper airway lumen to variable degrees. Therefore, the A/N ratio can be considered a useful objective tool in evaluating adenoid development in children. We aimed to investigate the growth and involution patterns of adenoids in consecutive age groups from birth to 16 years in Chinese children without SDB using MRI data, which may benefit the study of diseases associated with the development of adenoids.

The institutional review board of the Capital Institute of Pediatrics approved the present study (No. SHERLL2020039). Informed consent was obtained from each subject's parent, and assent was obtained from children aged >7 years.

During the more than 2-year study period, 680 Chinese children (out of whom 340 were male and 340 were female) with normal growth and development were selected from 2451 subjects who were invited to complete our sleep questionnaire and underwent head MRI, out of 18,934 patients undergoing MRI at our hospital from October 2017 to January 2020. The inclusion criteria were: (1) Chinese children ≤16 years old; (2) head MRI including all upper airway structures required for analysis; (3) no SDB as assessed by a standard questionnaire; (4) no medical history of surgery in the upper airway (adenoidectomy, tonsillectomy, or other); (5) no apparent deformities in maxillofacial soft tissue or bone; (6) no evidence of a brain tumor or brain anomaly and no motion artifact during imaging examination; and (7) no chronic respiratory disease such as asthma or bronchopulmonary dysplasia. Weight and standing height were recorded, and body mass index (BMI) Z-score was calculated in subjects aged above 2 years. BMI Z-scores are measures of relative

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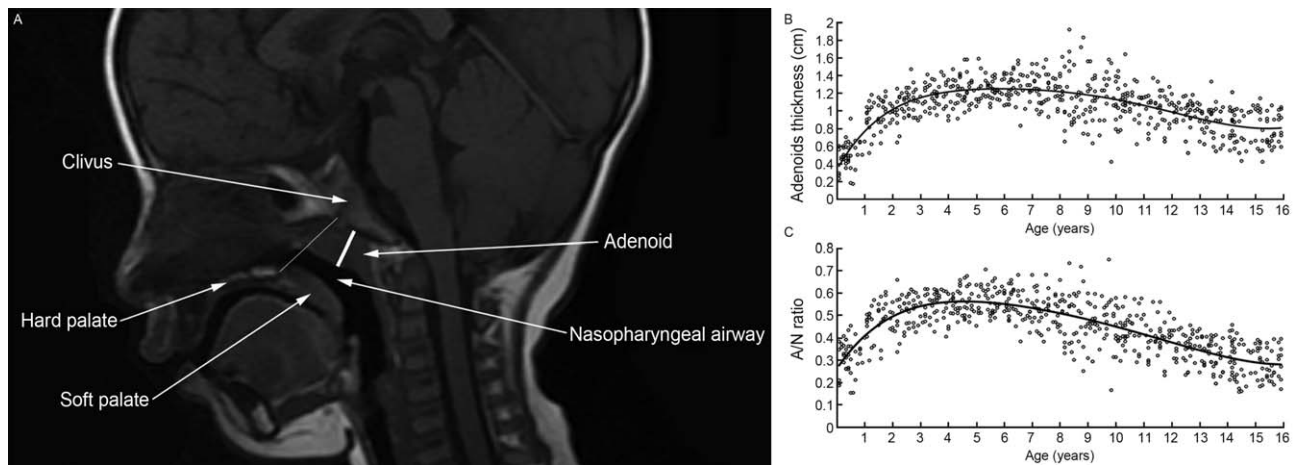


Figure 1: (A) Measurement methods of adenoids in mid-sagittal T1 weighted image. Adenoid thickness is measured along the line perpendicular from the point of maximal convexity on adenoidal to the line parallel to clivus base (thick white line). Bony nasopharyngeal height is the distance from the posterior-superior edge of the hard palate to the anterior-inferior edge of clivus (thin white line). (B) Curve fitting for the association of adenoid thickness with age. (C) Curve fitting for the association of A/N ratio with age. A/N ratio: Adenoid thickness/bony nasopharyngeal height.

weight adjusted for child age and sex. Subjects with a BMI Z-score between -1.645 and 1.645 were collected. Seventeen age groups were formed, ranging from birth to 16 years, with a 1-year interval. Each group comprised 20 males and 20 females.

A standard questionnaire regarding the symptoms of SDB used by our previous studies^[4,5] was applied to assess the likelihood of SDB in our population. MRI examinations were performed at the Department of Radiology, Capital Institute of Pediatrics, using a 1.5-Tesla Signa HDx scanner (GE, Healthcare, Waukesha, WI, USA). The studies were performed under sedation with oral chloral hydrate (50–100 mg/kg of body weight) in children under 6 years, whereas children above 6 years were in an awake state. The MRI scanning protocol was the same as our previous study.^[4] The image sets were reviewed and measured manually at an advantage workstation (AW 4.4 software; GE, Healthcare, Waukesha, USA). The midline sagittal slice was determined from the appearance of the corpus callosum and pituitary stalk. According to the method described in our previous study [Figure 1],^[4] two trained observers measured the adenoid thickness and bony nasopharyngeal height from the midsagittal T1-weight image of each subject; then, the A/N ratio was calculated.

Statistical analyses were conducted using SPSS (Version 22.0; SPSS, Chicago, IL, USA), and a P value < 0.05 was considered significant. First, a test of normality and homogeneity test of variance were performed. The adenoid thickness and A/N ratio were expressed as mean \pm standard deviation in each group. Linear regression analysis was performed to express the relationship between adenoid thickness, A/N ratio, and age. An independent sample t -test was used to analyze the statistical significance of the difference between males and females within each age group. The intra-class correlation coefficient (ICC) was computed to assess the inter-observers' agreement of interested variables.

The primary indications for head MRI were febrile convulsion ($n = 128$), headache ($n = 341$), head trauma ($n = 112$), vomiting ($n = 69$), and others ($n = 30$). None of these clinical indications confirmed the effect on the upper airway anatomy.

The adenoid thickness and A/N ratio distribution are listed in Supplementary Table 1, <http://links.lww.com/CM9/A528>. The ICC values for adenoid thickness and A/N ratio were statistically significant (ICC = 0.922, 0.976, $P < 0.001$, respectively), indicating good consistency between the two observers. There was no significant difference between females and males in each group except in the 14-year group.

The changes in adenoid thickness and A/N ratio from birth to 16 years are shown in Figure 1. The curve of adenoid thickness showed that they reach their maximum size at the age of 7 years and subsequently become smaller. Adenoid thickness increases rapidly between age of 1 to 2 years ($r = 0.799$, $P < 0.001$), increases slowly thereafter until age of 7 years ($r = 0.408$, $P < 0.001$), and then becomes progressively smaller ($r = -0.585$, $P < 0.001$). Similarly, the A/N ratio increases significantly with age under 6 years and decreases thereafter ($r = 0.691$, $P < 0.001$ and $r = -0.741$, $P < 0.001$, respectively).

Limited information exists on adenoid developmental patterns in children. This study revealed that adenoid development showed a peculiar pattern, differing from other lymphatic tissues such as the thymus and spleen. The gold standard in the diagnosis of SDB is polysomnography; however, it is not suitable for larger sample-sized research due to the time, effort, and expenses required. As with our previous studies,^[4,5] a standard questionnaire was used to screen the subjects to ensure the absence of SDB. We were confident that our subjects had no risk factors for SDB.

Consecutive age groups from < 1 year to 16 years were divided to investigate adenoid size in this study. Adenoids

in children without SDB were shown to have peak-thickness at 7 years, followed by an involution. Two previous studies evaluated the age-associated changes in the size of the adenoid and reported results in agreement with our findings. Cohen *et al*^[6] reported that adenoids have a unique pattern with a developmental peak in children from 5 to 8 years, followed by an involution based on CT data. Papaioannou *et al*^[3] reported that adenoids reach their maximum size at the age of 7 years (linear measurements) and subsequently become smaller, based on MRI data from 149 children without snoring.

This study showed that the A/N ratio in children without SDB reaches its peak value at the age of 6 years, suggesting it may be the period with the narrowest nasopharyngeal airway. No consensus exists on the A/N ratio in the general pediatric population. Papaioannou *et al*^[3] and Cohen *et al*^[6] reported that the A/N ratio increased to 8 years, with maximal value at the age group of 5 to 8 years, followed by a gradual decrease. However, a study showed a constant ratio of adenoid linear dimension to pharyngeal lumen diameter irrespective of age in children without snoring.^[2] The methodological characteristics likely explain the discrepant findings between previous reports and our study. First, we recruited more subjects with a broader age range than previous reports. Consecutive age groups allowed us to identify the A/N ratio in a detailed manner in children. Second, we created balanced age and sex groups in this study and strict inclusion criteria using a validated sleep questionnaire, which may benefit our results as being more representative. Cohen *et al*^[6] and our previous studies^[4,5] reported that the bony nasopharynx grew rapidly under 5 years and slightly increased between 5 and 8 years. This may explain this A/N ratio peak where adenoids grow faster than the bony nasopharynx, resulting in an increase in the A/N ratio at 6 years.

Few studies have addressed sex differences in adenoid development and A/N ratio. Our findings showed high consistencies of adenoid thickness and A/N ratio between females and males in most groups and confirmed the recent reports that assessed the thickness of the adenoids and tonsils using a methodology similar to ours.^[3] Only the 14 years' group showed a significant difference between sexes in the A/N ratio. The difference could be attributed to the relatively small sample in each age group. In our previous study,^[4] we reported that the upper airway length increased with the increase in body height, partly explaining why the A/N ratio was smaller in males >14 years, since male adolescents usually develop faster and are taller than females.

Our study had some limitations. First, it should be emphasized that MRI was performed under sedation in

children under 6 years, whereas children above 6 years undergoing MRI were awake. Second, the sample size of this study was insufficient; therefore, more clinical trials are needed to confirm our findings.

In conclusion, the present findings support the statement that adenoid development seems to differ from that of the rest of the body, showing a unique pattern. The adenoids reach their maximum size at the age of 7 years and subsequently become smaller. Furthermore, the normative values of adenoid size and A/N ratio after application of strict inclusion criteria, using a validated sleep questionnaire in Chinese children by MRI, have been established in this study. These data may serve as useful evidence in the management of SDB cases in this age group.

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Conflicts of interest

None.

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