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Measures of pituitary gland and stalk: from neonate to adolescence

Abstract

Objective: The aim of this study is to provide normative data about pituitary diameters in a pediatric population. Pituitary imaging is important for the evaluation of the hypothalamo-pituitary axis defect. However, data about normal pituitary gland diameters and stalk are limited, especially in children. Structure and the measurements of pituitary gland and pituitary stalk may change due to infection, inflammation, or neoplasia.

Methods: Among 14,854 cranial/pituitary gland magnetic resonance imaging scans performed from 2011 to 2013, 2755 images of Turkish children aged between 0 and 18 were acquired. After exclusions, 517 images were left. Four radiologists were educated by an experienced pediatric radiologist for the measurement and assessment of the pituitary gland and pituitary stalk. Twenty cases were measured by all radiologists for a pilot study and there was no interobserver variability.

Results: There were 10–22 children in each age group. The maximum median height of the pituitary gland was 8.48 ± 1.08 and 6.19 ± 0.88 mm for girls and boys, respectively. Volumes were also correlated with gender similar to height. Minimum median height was 3.91 ± 0.75 mm for girls and 3.81 ± 0.68 mm for boys. The maximum and minimum pituitary stalk basilar artery ratios for girls were 0.73 ± 0.12 and 0.59 ± 0.10 mm. The ratios for boys were 0.70 ± 0.12 and 0.56 ± 0.11 mm.

Conclusion: Our study demonstrated the pituitary gland and stalk size data of children in various age groups from

newborn to adolescent. It is thought that these data can be applied in clinical practice. Future prospective follow-up studies with larger samples, which correlate the structural findings with the clinical and laboratory results are awaited.

Keywords: children; normative data; pituitary size; pituitary stalk.

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Introduction

Magnetic resonance imaging (MRI) is the modality of choice in the evaluation of pituitary morphology and the use of this modality has increased dramatically over the last three decades (1). Pituitary stalk (PS) and pituitary gland (PG) abnormalities, such as empty sella, tumors, and midline malformations, can easily be assessed by MRI (2). However, assessment of some abnormalities, such as pituitary hypoplasia, might be difficult, therefore, normative data about PG and PS have become more necessary (3).

The PG forms in the sixth to seventh embryonic weeks and is situated in a protective sella turcica. The anterior PG arises from an invagination of the oral ectoderm and forms Rathke's pouch, whereas the posterior PG originates from neuroectoderm (4). The sizes of PG vary with age and physiologic status and it becomes its largest size during hormonally active conditions (such as puberty or pregnancy) (5, 6). In the literature, it has been reported that the height of the PG may reach 8 mm in pubertal boys (7). There are some reports about pituitary measurements in children with different age groups, however, these data pertain to a limited number of subjects and to low MRI technology (8, 9).

The PS shows similar changes depending on age and hormonal status (5, 6, 10–12). The ratio of PS to basilar

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artery (diameter) is used as a screening method for PS thickening and if the ratio is close to 1, further investigation is needed for tumoral thickening (e.g., germinoma, histiocytosis) (13). To the best of our knowledge, measurements of the PS in childhood and adolescence using 1.5- or 3-T MRI have not been studied until now. Accordingly, the aim of our study was to provide data regarding the PG size and PS/basilar artery (BA) ratio in healthy children according to age and gender.

Materials and methods

This study was submitted and approved by the Local Research Ethics Committee.

Subjects

Among 14,854 cranial/pituitary MRI scans performed from 2011 to 2013 in our center, 2755 MR images of Turkish children aged 0–18 were acquired. After reviewing the relevant patient files, three pediatricians excluded those patients' MR scans ($n=1947$) who had endocrinologic abnormality, history of asphyxia or short-term delivery at <35 weeks, breech presentation, or abnormal MRI findings. Thereafter, the MR images were reviewed by four radiologists and 291 were excluded due to additional radiologic abnormalities. Eventually, we were left with MR images of 517 children (who had undergone MRI for idiopathic headache and idiopathic epilepsy).

MR measurements

Four radiologists (S.S., V.A., E.O., and S.I.) were initially trained for the measurements by a pediatric radiologist (M.K.) experienced in cranial/pituitary MR assessment. Before performing the measurements, we selected 20 patients for a pilot study. In the pilot study, four radiologists performed all measurement and discussed the difference between them. They worked on this issue until they have reached a consensus on measurements. At the beginning, 120 randomly selected patients were evaluated by all radiologists to determine interclass correlation coefficient as an interobserver reliability measure. Then, all 517 images were examined by one of the four radiologists. The flowchart diagram of the study is given in Figure 1.

Measurements

The PG and PS were measured on mid-sagittal and coronal images (Figure 2A). The coronal width and height of PG were evaluated on coronal images. Sagittal width of the PG is shown in Figure 2B. PG volume was calculated with the $\text{height} \times \text{coronal width} \times \text{sagittal width} \times 0.5$ formula (1). The diameters of the PS and BA were measured on axial images on the same plane in the middle of the PS (Figure 2C). PS/BA ratio was calculated.

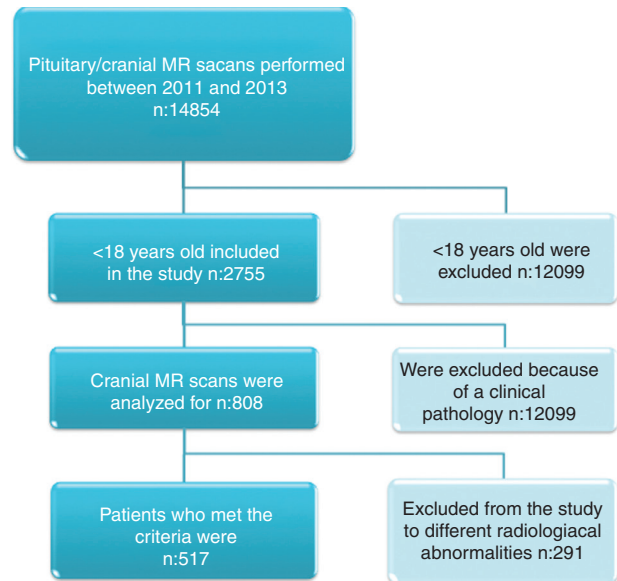


Figure 1 Flowchart of the study group.

MR Acquisitions

All MR examinations were performed with 1.5-T (Symphony; Siemens, Erlangen, Germany) or 3-T MR scanners (Achieva; Philips, Amsterdam, The Netherlands) by using a head coil. Three-tesla MRI equipment has better signal-noise ratio and temporal resolution. Field strength effects almost every imaging parameter, therefore, we used different imaging parameters in 1.5- and 3-tesla equipment and we gained images with identical slice thickness. However, the acquisition time was lower in 3-tesla MR equipment due to its high magnetic field strength. The signal intensities of the lesions, such as hematoma, may differ in the two scanners, but the anatomical structures appear identical. Patients were imaged in the supine position. Conventional MR examination lasted approximately 25 to 30 min for each patient. The vast majority of the measurements were performed on multiplanar reformatted images if 3D T1 sequence was performed [repetition time (TR)/echo time (TE), 8.3/3.8 ms; flip angle, 8°; slice thickness, 1 mm). In those cases with suboptimal 3D T1 images due to motion or various types of artifacts and without 3D T1 sequence, the measurements were performed on T1 sagittal images (TR/TE, 700/10 ms; flip angle, 70°; slice thickness, 2 mm); T2 axial images (TR/TE, 3000/80 ms; flip angle, 90°; slice thickness, 2 mm); and coronal SPIR images (TR/TE, 3000/80 ms; flip angle, 90°; slice thickness, 2 mm).

Statistical analyses

Before the measurement step, the inter-rater reliability was evaluated by inter class correlation coefficients (ICC). Researchers were informed about ICC of different measurement criteria and a discussion section was performed to increase accuracy. The measurements were mean $\pm$ standard deviation in the scale of mm. Statistical analyses were performed by SPSS for Windows version 15.0 (SPSS Inc., Chicago, IL, USA) and results visualized by Microsoft Office Excel program (Microsoft Corp, Redmond, WA, USA). Mean and standard errors calculated

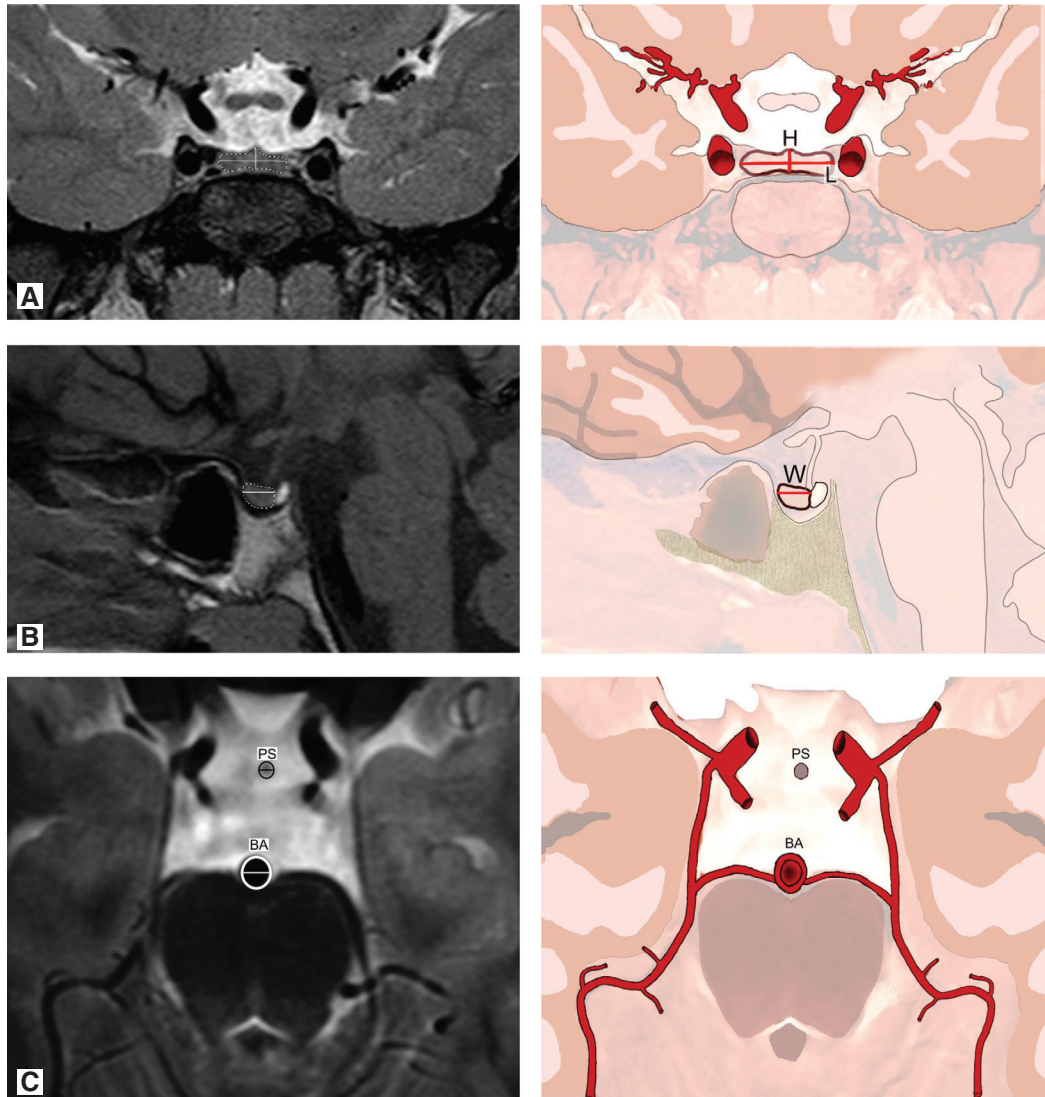


Figure 2 (A) Height and coronal width of the pituitary gland on coronal plane. (B) Width of the pituitary gland on sagittal plane. (C) Pituitary stalk and basilar artery on axial plane.

for each age groups and genders. Scatter charts were drawn with ± 2 standard error values besides means. Drawn lines smoothed according to the best regression curve. Independent samples t-test was used to compare pituitary dimensions between male and female groups. A p-value < 0.05 was considered statistically significant.

Results

There were 10–22 children in each age group and there were 517 children in total, with 261 girls. Pituitary diameters, volume and PS thickness were determined in all subjects. All PG dimensions were showing an increase with advancing age. Due to different findings between girls and boys, the results were given separately by gender. The median height of the pituitary gland was 3.81 ± 0.68 and 8.48 ± 1.08 mm

for girls in the younger than 1-year-old group and 18-year-old age group, respectively, for boys, it was 3.91 ± 0.75 and 6.19 ± 0.88 mm, respectively. The maximum and minimum PS/BA for girls were 0.73 ± 0.12 mm in younger than 1-year-old age group and 0.59 ± 0.10 mm in the 8-year-old age group. The ratios for boys were 0.70 ± 0.12 mm in the 18-year-old age group and 0.56 ± 0.11 in the 9-year-old age group. The results are shown in Tables 1 and 2. Figures 3 and 4 include diagrams for the standard deviation scoring system.

Discussion

In this study, we have reported the MRI data of the pituitary gland and stalk in healthy children from neonate

Table 1 Pituitary gland diameters and volumes; pituitary stalk/basilar artery (PS/BA) ratio in girls.

Age	n = 261	Pituitary height	Pituitary coronal width	Pituitary width	Pituitary volume	PS/BA
<1	14	3.81±0.68	8.82±1.02	4.37±0.43	73.86±17.99	0.73±0.12
1	15	4.68±0.62	10.04±1.22	4.99±0.79	119.03±36.5	0.64±0.10
2	10	4.48±0.82	9.37±2.94	4.93±0.58	102.62±44.64	0.64±0.13
3	13	4.25±0.68	11.45±1.39	4.76±0.67	116.02±29.82	0.61±0.14
4	12	4.37±0.92	11.30±1.81	5.85±0.61	141.83±28.92	0.62±0.14
5	14	4.96±0.91	11.29±1.48	5.67±0.84	158.81±40.88	0.61±0.08
6	12	3.82±1.06	11.58±1.67	5.40±0.72	121.41±45.29	0.62±0.13
7	14	4.26±1.25	12.30±1.53	5.44±0.50	146.39±55.40	0.60±0.10
8	13	4.63±1.30	11.84±1.82	6.11±0.81	167.23±55.98	0.59±0.10
9	10	4.43±0.92	12.96±1.84	5.99±0.89	172.44±56.35	0.65±0.13
10	10	5.09±1.36	11.81±1.69	6.19±1.05	191.87±80.94	0.59±0.13
11	11	4.75±0.76	13.26±1.59	6.22±1.16	198.92±61.80	0.65±0.10
12	13	4.92±1.51	13.13±2.02	6.91±1.09	238.57±144.5	0.65±0.15
13	21	6.15±1.09	14.21±2.32	7.43±1.27	329.75±105.01	0.62±0.13
14	16	6.00±1.02	14.50±1.21	7.26±1.05	320.87±99.41	0.64±0.10
15	17	6.18±1.01	13.62±1.90	7.57±0.84	325.54±106.96	0.61±0.11
16	18	7.42±1.18	13.93±1.53	6.14±1.02	318.37±83.33	0.65±0.13
17	17	8.09±1.23	13.69±2.08	5.82±1.26	323.57±97.45	0.63±0.14
18	11	8.48±1.08	13.95±1.89	5.90±1.09	349.95±93.77	0.65±0.15

to adolescent. Although MRI of the pituitary gland is advocated as part of the essential investigations to be performed in children with diagnosis and follow-up of those endocrine diseases, its interpretation as regards the pituitary imaging is difficult and subjective. Therefore, standardization in these diameters are considered necessary.

Craniocaudal, transverse, and anteroposterior diameters are named as height, coronal width, and width, respectively. Indirect volume calculations were performed for pituitary volume, height×coronal width×width×0.5 derived from the volume calculation of ellipsoid (1). However, the shape of PG can be disrupted due to pituitary pathologies and ellipsoid appearance might be distorted.

Table 2 Pituitary diameters and volumes, pituitary stalk/basilar artery (PS/BA) ratio in boys.

Age	n = 256	Pituitary height	Pituitary coronal width	Pituitary width	Pituitary volume	PS/BA
<1	13	3.91±0.75	9.62±1.06	4.68±0.59	88.70±25.71	0.65±0.12
1	14	3.77±0.50	10.02±1.77	4.83±0.67	92.64±31.24	0.63±0.05
2	13	4.17±0.77	11.22±1.48	5.48±2.06	127.94±51.03	0.62±0.09
3	11	4.50±0.81	10.47±0.89	5.00±0.83	118.67±34.67	0.60±0.06
4	14	4.63±0.96	11.69±1.09	5.41±0.94	147.79±48.61	0.64±0.08
5	15	4.32±0.80	11.99±0.96	5.89±0.93	153.79±39.68	0.59±0.08
6	10	4.56±0.89	11.00±1.62	6.31±0.96	157.54±43.52	0.62±0.10
7	17	4.59±1.20	11.97±1.30	5.90±0.66	163.25±51.52	0.60±0.09
8	11	5.05±0.75	11.75±1.55	6.47±0.92	195.21±61.63	0.58±0.08
9	12	4.14±0.87	12.66±1.98	5.90±0.52	153.77±39.95	0.56±0.11
10	12	4.24±1.20	12.62±1.80	6.26±1.09	167.81±63.37	0.57±0.13
11	13	4.45±1.14	12.57±1.39	6.04±0.99	171.11±59.81	0.56±0.11
12	15	4.22±1.17	13.04±1.88	6.19±1.21	172.82±71.92	0.60±0.12
13	10	5.33±0.81	13.55±1.06	6.53±0.56	237.32±52.65	0.64±0.11
14	17	5.24±1.08	13.66±1.79	6.59±1.16	237.17±78.71	0.60±0.09
15	14	5.05±1.62	13.77±1.34	6.58±1.59	242.39±124.01	0.60±0.15
16	22	5.13±1.22	13.73±1.31	7.20±1.13	256.29±91.66	0.67±0.11
17	11	5.24±0.88	13.62±1.54	8.12±1.32	286.88±63.11	0.67±0.12
18	12	6.19±0.88	12.98±1.94	7.46±1.07	305.43±98.30	0.70±0.12

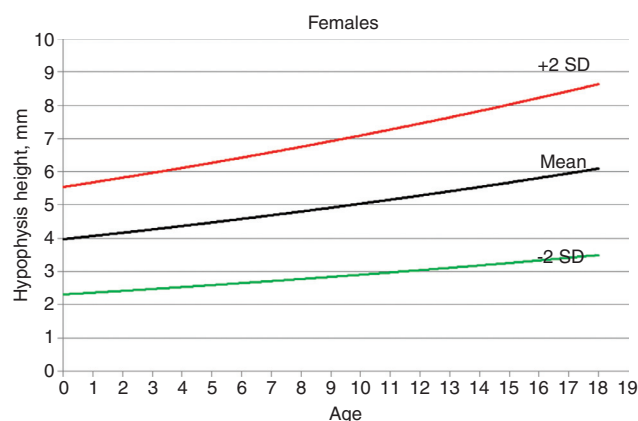


Figure 3 Pituitary height plotted against age for girls.

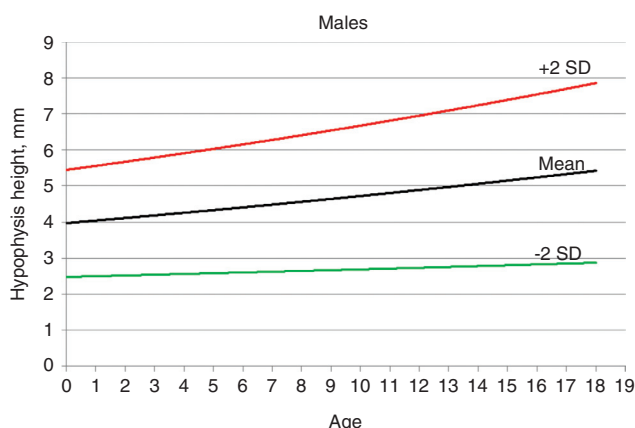


Figure 4 Pituitary height plotted against age for boys.

In these circumstances, the formula can cause misinterpretation. In general, pituitary height is accepted to reflect pituitary growth. During puberty, there is a spike of pituitary height followed by a plateau when it reaches adult values. In our study, increasing time of PG volume and height was 11 years old for girls and 13 years old for boys. The time was consistent with pubertal onset. Again, in our study, the PG size was significantly larger in girls than in boys, which was similar to the study of Takano et al. (14). Although volumetric studies from indirect volume calculation had some different results (15, 16), we suggest that this simple formula can be used to predict the pituitary volume.

PS also shows similar changes depending on age or physiologic status, such as PG dimensions (5, 6, 10–12). Many pathologic entities have been shown to lead enlargement of the PS, including diabetes insipidus due to histiocytosis and other causes, such as tumors, metastases, sarcoidosis, and infections. Therefore, assessment of the normal appearance of the PS is important for an accurate diagnosis. The appearance of PS lesions may be a radiologic challenge, therefore, standardization of the PS diameter is also necessary. The PS to BA ratio is a readily applied visual screening tool that enables easy recognition of the possibly abnormal PS and ratio close to one should alert the clinician. Classically accepted PS to BA ratio is <1 and our results support this ratio where maximum ratios were 0.73 and 0.70 in girls and boys, respectively.

The main limitation of our study is its retrospective style of reviewing previous MR scans. There has not been any consideration concerning the clinical and laboratory data of the subjects. Another minor drawback could be the lack of percentile curves (for age and sex) that was due to an insufficient number of subjects for such an analysis.

In conclusion, our study demonstrated the PG size and PS thickness data of children in various age groups

from newborn to adolescent. Future prospective studies with larger samples that correlate the structural findings with the clinical and laboratory results are awaited.

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