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Assessment of Normal Pituitary Gland Volume in Paediatric Population Using MR Volumetry - A Single Centre Experience

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Abstract: ***Accurate assessment of pituitary gland size is important in children with suspected endocrine disorders, yet routine evaluation based on gland height may overlook normal differences in shape and anatomy. This cross-sectional study estimated the true pituitary gland volume in healthy Indian children younger than 12 years using direct manual measurements on sagittal T1 weighted MRI images. Seventy-one children with normal pituitary function and normal brain MRI findings were included after careful clinical screening. Pituitary volume and mid sagittal height were measured and analysed according to age and sex. The results showed a gradual increase in pituitary volume with age in both boys and girls, with the highest values observed between 10 and 12 years. A significant sex difference was noted only in this age group, while gland volume remained largely independent of sex during earlier childhood. The measured values were broadly comparable with findings from previous studies, although some differences were observed in older children, possibly reflecting ethnic variation. The study provides preliminary reference values for pituitary gland volume in Indian children and supports the use of direct volumetric MRI assessment as a more reliable approach for evaluating normal pituitary size.***

Keywords: pituitary gland, magnetic resonance imaging, pituitary volume, pediatric population, endocrine assessment

1. Introduction

The pituitary gland is aptly known as the leader of the endocrine orchestra despite its small size, playing a key role in the growth, metabolism and reproductive function. Slight variations in the overall size of the gland can have profound impact on other neuroendocrine organs contributing to a wide spectrum of disorders. Hence the pituitary gland has been an area of interest for researchers worldwide.

Magnetic resonance imaging (MRI) of the pituitary gland is advocated as part of baseline investigations to be performed on children with idiopathic short stature or suspected endocrine dysfunction (1–9). Recognition of abnormalities in the pituitary size can however be challenging owing to the variable morphology of the gland which does not conform to any known geometrical figure and more often radiology reports of pituitary gland size are based upon subjective assessment. Variations in the contour of the gland and sella turcica cannot be considered as reliable indicators of pituitary gland abnormality as the anatomy of this region is highly variable even in normal subjects.

Majority of pituitary gland measurements are focused on height, which is considered to be the standard indicator for pituitary gland size. However, Considering the wide variations in the morphology of the normal pituitary gland with age, gender, ethnicity and hormonal status(3,10–15), any assessment of its size will be subject to a lack of precision. This prompts the ***need for a more reliable measure such as the true volume*** of the gland so that subtle variations from normal can be picked up.

The Growth Hormone Society summary statement of 2000 indicated the need for more data on normal pituitary dimensions (9). ***There is dearth of useful literature to serve as reference standard for the normal range of pituitary volumes in Indian paediatric population (1,9)***. Most reports available to date on the size of the normal pituitary gland are obtained from indirect methods of volume estimation (16). More recently, few foreign studies have calculated volume by direct measurement using thin section 2D and 3D MR images (17,18).

It is known that the pituitary gland volumes may vary with ethnicity and also among different races. With respect to Indian population, only few studies have attempted estimation of true volume by direct methods with limited studies on paediatric population. We share our experience at estimating pituitary volume using this novel method.

2. Methods

a) **Study Design:** Cross sectional study

b) **Study Setting:** Dept. of Radio-diagnosis, Dept. of Paediatrics, Govt. Medical College, Kozhikode

c) **Study Subjects:** After meticulous history taking and detailed physical examination, children below 12 years of age undergoing MR imaging of brain for non- pituitary related causes such as evaluation of headache, idiopathic developmental delay or seizures were enrolled to the study. Written informed consent obtained from parents/guardian before the child' participation.

Inclusion Criteria

- Children under 12yrs of age with clinically normal pituitary function and normal MRI report.

Exclusion Criteria

- Children with known endocrine and neuropsychiatric diseases which are thought to influence the pituitary gland volume were excluded from the study.
- Children with history of or clinical evidence of genetic syndrome, birth asphyxia, cranio-spinal irradiation, preterm delivery were excluded.
- Those with any abnormal findings on MR imaging also were excluded.

Clinical examination:
All study subjects underwent detailed physical examination including anthropometric measurements before MRI. Digital scale and stadiometer was used to record weight, and height and BMI calculated using the formula weight/height2. Patients with extreme values of height were excluded from the study as height is considered the most appropriate indicator of subclinical endocrinopathy.

d) Sampling Procedure
- Sampling Population: All patients fulfilling inclusion and exclusion criteria.
- Sample Size Calculation:

Standard deviation of mean pituitary volume in males aged between 11 and 20yrs in a previous study by Joish Upendrakumar and Kavitha Y is 1.26.

The formula used for determining sample size is given below:

$$Z\sigma^2\, n{=}(\mathrm{E})$$

where **Z** = 1.96 for 95% CI, **σ** is the standard deviation of the outcome variable and **E** is the desired margin of error (critical value x standard deviation= 0.3).

Sample size estimated using the above calculation is 71.
(iii) 3- SAMPLING TECHNIQUE: Convenient sampling

Study Period
After receiving ethics approval, data was collected over a period of 18 months.

e) Study Procedure

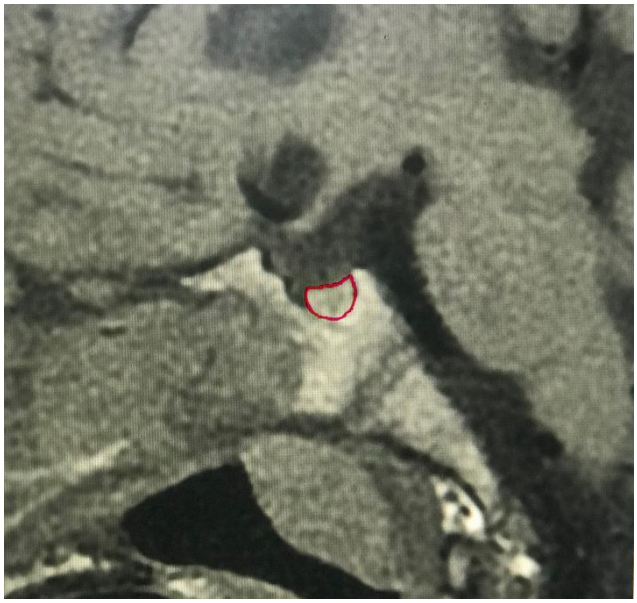
Imaging Techniques
- MRI examination of all subjects was performed using 1.5T clinical signa scanners (GE health care) with an 8-channel head coil.
- T1 weighted images were utilized as they are best for anatomic depiction.
- T1 weighted sagittal spin echo acquired with TR =1180ms and TE = 10.9ms. Initially, thin (0.9mm) slices were acquired for volume estimation. However, the technique had to be modified to 2mm thick slices of the gland owing to increased noise with the thinner slice images. Small field of view (24x24cm) images constructed on 256X256 matrix was used.

Table 1: MRI Protocol

Sequence	T1 weighted image
Plane of image acquisition	Sagittal
Slice thickness	2mm
TR	1180ms
TE	10.9ms
Matrix size and Field of view	256x256, 24 x 24cm

Measurements
Pituitary gland was manually traced using the area tool for irregular shapes in T1 weighted sagittal images employing all sections in which the gland was seen.

Pituitary gland volume (in mm3) was then obtained by adding areas of the gland in all slices and multiplying by a factor of 2 (slice thickness of images being 2 mm) This method of volume estimation was similar to that employed by Takano K et al (18)



Manual tracing of the pituitary gland in sagittal T1 weighted image

Pituitary height was estimated from mid sagittal sections as the straight-line distance from the midpoint of the adenohypophysis on the superior surface to the bottom edge of the gland.

f) Analysis of Observations
- The data obtained is grouped into class intervals based on age and sex for analysis.
- Statistical analysis done using the SPSS software and Microsoft excel.
- Mean and standard deviation for all collected data calculated and expressed using tables and graphs and Pearson's correlation to assess the relationships between age, sex and pituitary dimensions.
- Minimum level of statistical significance was set at $P < 0.05$

3. Results

According to the present study, pituitary gland volume shows an increasing trend with age in both genders, maximum volume recorded is between 10-12 years. There is statistically significant difference between gland volume and gender in this particular age group (10-12yrs). Otherwise, the mean gland volume appears to be gender independent.

Table 2: Mean volume of the pituitary gland in different age groups

Age Group	Boys		Girls	
	Mean Pituitary Gland Volume (mm^3)	SD (mm^3)	Mean Pituitary Gland Volume (mm^3)	SD (mm^3)
0-2 yr	160.5	552.05	165.5	43.36
2-4 yr	183	33.31	193	31.06
4-6 yr	223	15.72	215	19.17
6-8 yr	258	2.49	273	3.99
8-10 yr	325.5	20.3	340.5	38.77
10- 12 yr	380.5	47.32	408	65.09

4. Discussion

The normal gland exhibits a diverse range of morphology and its dimensions vary considerably, being influenced by age, sex and hormonal environment. There appears to be positive correlation between the volume of the gland and endocrine dysfunction which imparts clinical significance to the estimation of gland volume. With widespread use of neuroimaging in children with short stature and other clinical indicators of endocrine dysfunction, detection of subtle alterations in the gland assumes great significance. However, scant data on the normal dimensions of the gland for each age group is lacking which makes the task at hand daunting. Roldan-Valadez *et al* (20) hypothesized that the traditional geometric method should be replaced by 3D volumetric measurement that had higher accuracy and smaller discrepancy. Available data are mostly based upon indirect methods of volume estimation which lacks precision owing to the fact that the gland exhibits varied morphology and does not conform to any known geometrical figures.

In this study, we aimed to report the normative data on pituitary gland volume in Indian paediatric population (0-12 years). Additionally, the morphology of the superior surface of the gland, mid sagittal height, presence of posterior pituitary bright spot was assessed.

It was observed that the mean volume and mid sagittal height of the gland demonstrated a linear increase with age. The calculated volumes and mid sagittal height were comparable to those obtained by Han et al (3) in 75 healthy Chinese children. Between 0-8 years, the measured volume in our study was in agreement with that of Fink et al in an ethnically diverse population of children. However, the volume of the pituitary gland appeared to differ between Indian population and western population between 10-12 years. The reasons for the difference could be due to sample sizes or ethnic differences. A comparison of our results with the other two studies has been shown in the table.

Table 3: Comparison of our results (mean pituitary volume in mm^3) with previous studies

Age Group	Present Study		Age Group	Han et al in Chinese population		Age Group	Fink et al in a mix of western and south Asiam population
	Boys	Girls		Boys	Girls		
0-2	160.5	165.5	1-4	229.2	217.9	1-2	174- 184
2-4	183	193				3-4	193- 203
4-6	223	215	5-9	322.3	358	5-6	214- 226
6-8	258	273				7-8	237- 250
8-10	325.5	340.5	10-14	474.4	606.1	9-10	263- 277
10- 12	380.5	408					

A comparison between the volume of gland in both sexes of each group was done to look for any relationship between gender and mean volume. On analysing the different age groups, it was seen that the mean volume of the pituitary gland in girls was slightly larger than boys in all age groups, except between 4-6 years. This difference was however, not found to be statistically significant except between 8-12 years implying that the overall mean gland volume is independent of gender in prepubertal age group.

This observation was in concordance with the study by Fink et al in which there was no significant gender related variations in the gland volume in prepubertal children. Study by Takano et al also revealed no association between volume of the whole gland and gender up to 9 years, beyond which the volume in girls was significantly greater than in boys.

5. Conclusion

Direct MRI based measurement of pituitary gland volume offers a practical and reliable way to assess gland size in children, especially when normal anatomical variation makes height-based evaluation less dependable. Pituitary volume increased steadily with age, while differences between boys and girls became noticeable only in the older age group. The reference values generated in this study provide useful baseline information for the Indian paediatric population and may assist in recognizing subtle abnormalities during endocrine evaluation. Larger multicentre studies are needed to strengthen these findings and develop widely accepted reference standards.

What is already known? There is positive correlation between pituitary gland size and endocrinopathy and that direct measurement of the gland volume alone is an accurate indicator of gland size.

What this study adds? The normative data for pituitary gland volume estimated by direct method is limited for the Indian population and it is known that ethnicity influences pituitary gland volume. This study sets the base for a future research involving larger sample to establish standard of reference for pituitary measurements in the Indian paediatric population.

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