Original Article

Study of Pituitary Morphometry Using MRI in Indian Subjects

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Abstract

Aim: To establish normative measurements of pituitary gland in Indian population. **Material and Methods:** In this cross-sectional study, we measured dimensions of pituitary gland in 482 (213 females and 269 males) Indian subjects with apparently normal pituitary gland function. Mid-sagittal T1-weighted image (T1-WI) on magnetic resonance imaging (MRI) was used to measure height and length of pituitary gland. Pituitary gland width was measured using coronal T1-WI and pituitary gland volume was calculated. **Results:** Mean height, length and calculated volume of pituitary gland was significantly higher in females compared to males (p = <0.001, P = 0.03 and P = <0.001, respectively) when all age groups were combined but pituitary gland width was not statistically different in male and female subjects. When subjects were divided into different age groups, except for 10–14 years age group where pituitary height was significantly higher in females as compared to male, no significant difference was observed between male and female in any of the parameters (height, length, width and volume). The mean pituitary gland height was 5.80 ± 1.32 mm and 5.37 ± 1.25 mm in female and male subjects, respectively. Females achieved peak pituitary gland height in 10 to 14-year age group, while males achieved their peak pituitary gland height in 15 to 19-year age group. **Conclusion:** Our study provides age and sex wise normative data for pituitary measurements derived from Indian population.

Keywords: Indian subjects, magnetic resonance imaging, pituitary measurements

Introduction

Radiological imaging of the hypothalamic-pituitary region before availability of magnetic resonance imaging (MRI), was based on the plain radiographs and computed tomography (CT) scan of skull. But in current medical practice, MRI has been accepted as the imaging modality of choice for visualizing the intracranial structures including pituitary gland due to its numerous advantages over other modalities. Earlier studies have described dynamic changes in the size, shape and signal intensity of the pituitary gland with age.[1–3] There are variations among normative data described by different authors.[3–6] Though, there are numerous studies on pituitary morphometry, they all have inherent limitations like including subjects of only narrow age range and subjects with intracranial pathologies which could have potentially affected pituitary gland size. As a result, there is no consensus on normal pituitary gland measurements. With this background, we designed this project to study the age and sex-related changes in pituitary gland size and morphology in a cohort of Indian population.

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Materials and Methods

This cross-sectional study was conducted at the All India Institute of Medical Sciences (AIIMS), New Delhi between March 1, 2015 and July 15, 2016 (inclusive). All inpatients at AIIMS, who underwent MR imaging of brain during study period, were screened for their eligibility to be included in this study on the day of MR imaging itself. Patient's medical records were scrutinized to see indication of MRI and to ensure that they did not have medical conditions influencing pituitary size (as mentioned below in exclusion criteria). Permission from the institutional ethics committee of AIIMS was obtained before starting the study.

Exclusion criteria:

Subjects with any of the following clinical conditions were excluded from the study – (1) subjects with history of

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any pituitary diseases in past or present, (2) subjects who received in past or receiving at present, hormonal therapy, including thyroxin, gonadal steroids and adrenal steroids (except use of corticosteroid for <7 days before current MRI, and not prescribed for adrenal insufficiency), (3) subjects with history of any psychiatric disorder or receiving antipsychotic drug, (4) subjects with history of intracranial surgery or radiation at any point of time in life, (5) subjects with history of breech delivery or birth asphyxia, (6) subjects with pregnancy and post-partum less than two weeks, (7) subjects with any structural abnormality in the pituitary hypothalamic region on MRI (pituitary cyst, adenoma, partial empty sella, tumors invading sella), (8) subjects whose MRI findings were suggestive of increased intracranial pressure, (9) subjects with MRI findings suggestive of perinatal insult.

Measurements were made by two qualified radiologists with minimum of 10 years of experience in MRI reporting (DK and AG), independently with subsequent discussion if required to minimize variation in observations.

MRI study and pituitary measurements

MRI scans were performed on 1.5 Tesla (Avanto, Siemens, Erlangen, Germany) or 3 Tesla (Achieva or Ingenia, Philips Medical Systems) MR unit. Pituitary gland measurements were performed as earlier described by Argyropoulou *et al.*[7]. Measurements of pituitary gland height and length were performed in the mid-sagittal T1-WI using electronic cursor on a work station. Mid-sagittal section was defined by visualization of the anterior and posterior pituitary lobes with pituitary stalk in the same slice. Height of the pituitary gland was measured at the site of insertion of stalk as the maximum vertical distance between the upper and the lower border of the gland as shown in Figure 1. Pituitary gland's length was measured as the maximum antero-posterior extent of the gland in horizontal plane. Pituitary gland width was measured as the maximum transverse diameter of the pituitary in coronal T1-WI showing pituitary stalk. Pituitary volume was calculated using Di Chiro's formula, that is, volume = 1/2 × height × length × width.[8] Shape of the superior surface of pituitary gland was described as either flat, concave or convex upper border in midline sagittal T1-WI.

Statistical analysis

Data were analyzed by using Statistical Package for Social Sciences (SPSS) software, version 23 (SPSS Inc., Chicago, IL, USA). Continuous variables are described in terms of mean ± standard deviation (SD) or median with interquartile range.Categorical variables are described in the form of frequency and proportion. Intergroup differences were analyzed by using student's t-test, Mann–Whitney U test and Chi-square test as appropriate. A *P* value of <0.05 was considered to be statistically significant.

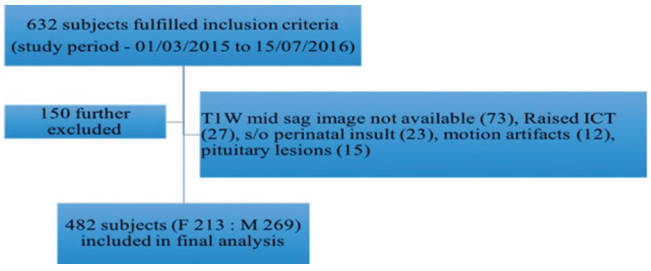

Figure 1: Enrollment of study subjects

Results

Total of 632 subjects were found to be eligible for the enrollment in this study, after screening all inpatients who underwent MR imaging of brain during the study period. One hundred and fifty subjects were further excluded from the study for various reasons [Figure 1]. Four hundred and eighty-two subjects (269 males and 213 females) were included in the final analysis. Table 1 shows pituitary gland measurements of study population. Data were further stratified into 20 groups on the basis of age and sex of study subjects. Subjects of each sex were arbitrarily divided into 10 age groups as shown in Table 2.

Pituitary gland height was greater in females than males for all age groups, except in age group of ≥50 year, as shown in Table 2. Spurt in the pituitary gland height was noted during second decade of life in both sexes [Figure 2]. Females achieved peak pituitary gland height earlier than males. Pituitary gland height decreased gradually in both sexes after achieving its peak during second decade of life.

Table 1: Pituitary gland measurements in male and female subjects

Pituitary dimension	Sex	No. of subjects	Mean±SD	*P*
Height (mm)	F	213	5.80±1.32	<0.001
	M	269	5.37±1.25	
Length (mm)	F	213	9.37±1.56	0.03
	M	269	9.05±1.65	
Width (mm)	F	210	12.77±2.18	0.23
	M	264	12.54±2.00	
Volume (mm^3)	F	210	354.98±130.60	<0.001
	M	264	313.45±123.54	

F: Female, M: Male, *P* - value for difference between male and female subjects, SD: Standard deviation, mm: Millimeter

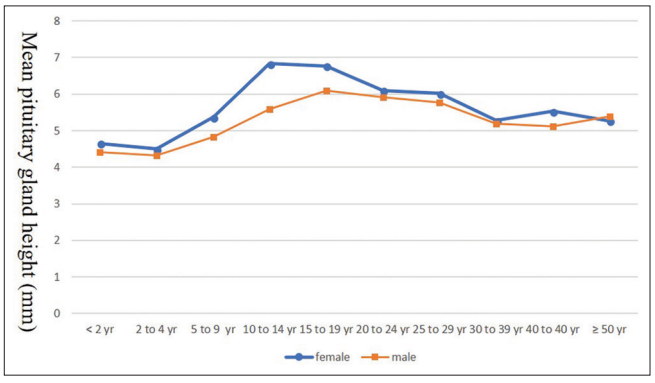

Figure 2: Age and sex wise mean height of pituitary gland

Differences in pituitary gland length, width and volume between the two sexes was not statistically significant for any of the age group. Females in age group of ≥50 year had maximum length (10.31 ± 1.32 mm) of pituitary gland, whereas maximum length of pituitary gland in males (10.01 ± 1.56 mm) was observed in 40 to 49-year age group [Table 3]. Maximum pituitary gland width was 13.67 ± 2.27 mm and 13.19 ± 1.83 mm in females (30–39 year) and males (40 to 49 year), respectively [Table 4]. Pituitary gland width was higher in male subjects up to age of 14 years, after that it was higher in female subjects but difference was not significant. Calculated pituitary gland volume was higher in females in all age groups, except 2 to 4-year age group [Table 5]. Spurt in the pituitary gland volume was noted in the second decade of life in both sexes.

Overall, most frequently observed shape of the superior surface of pituitary was concave (209 subjects, 43.4%). Total of 85 (17.6%) subjects had pituitary gland with convex superior

Table 2: Pituitary gland height for different age-sex groups

Age group (year)	No. of subjects (F/M)	Pituitary gland height in mm (mean±SD)		*P*	Pituitary gland height range in mm (max-min)	
		Females	Males		Females	Males
<2	6/11	4.65±0.49	4.41±0.73	0.50	4.0-5.2	3.0-5.6
2-4	9/17	4.50±0.80	4.33±0.52	0.55	3.2-5.9	3.4-5.4
5-9	19/23	5.37±0.97	4.83±1.05	0.09	4.0-7.0	3.0-6.6
10-14	22/21	6.83±1.30	5.58±1.40	0.004	4.8-9.8	3.0-8.8
15-19	26/43	6.77±1.54	6.10±1.24	0.051	4.6-10.0	3.6-10.0
20-24	23/25	6.10±0.88	5.92±1.35	0.60	4.8-8.0	3.6-9.5
25-29	22/23	6.02±1.21	5.76±1.11	0.45	3.0-8.1	3.5-8.0
30-39	28/28	5.28±1.05	5.19±1.26	0.77	3.5-7.4	3.1-8.4
40-49	22/28	5.53±1.23	5.11±1.08	0.21	3.5-7.6	3.0-7.0
≥50	36/50	5.27±1.14	5.38±1.21	0.66	3.3-8.0	3.0-9.0

Table 3: Pituitary gland length for different age-sex groups

Age group (year)	Female		Male		*P*
	No. of subjects	Length in mm	No. of subjects	Length in mm	
<2	6	6.86±1.69	11	6.42±0.74	0.61
2-4	9	6.98±0.78	17	7.09±1.37	0.84
5-9	19	7.50±1.08	23	7.41±1.12	0.80
10-14	22	8.62±1.39	21	8.35±1.51	0.53
15-19	26	9.74±1.40	43	9.26±1.04	0.10
20-24	23	9.62±1.30	25	9.37±1.41	0.52
25-29	22	9.85±1.12	23	9.63±1.49	0.57
30-39	28	9.53±1.18	28	9.77±1.18	0.46
40-49	22	10.20±1.01	28	10.01±1.56	0.63
≥50	36	10.31±1.32	50	9.79±1.25	0.07

Table 4: Width of the pituitary gland for different age-sex groups

Age Group (year)	Female		Male		*P*
	No. of subjects	Width in mm	No. of subjects	Width in mm	
<2	5	8.18±1.34	11	9.73±1.47	0.06
2-4	8	10.77±1.97	17	11.60±1.96	0.35
5-9	19	10.92±1.17	23	11.54±2.00	0.23
10-14	21	12.62±2.05	21	12.86±2.62	0.74
15-19	26	13.29±1.80	40	13.14±1.63	0.73
20-24	23	13.43±1.89	25	12.70±1.56	0.14
25-29	22	13.22±1.66	23	12.77±1.63	0.36
30-39	28	13.67±2.27	28	13.03±1.64	0.23
40-49	22	13.50±2.15	28	13.19±1.83	0.57
≥50	36	12.68±2.03	48	12.48±2.10	0.66

Table 5: Age and sex wise calculated volume of the pituitary gland

Age Group (years)	Female		Male		*P*
	No of subjects	Volume in mm^3	No. of subjects	Volume in mm^3	
<2	4	141.86±71.60	11	140.33±40.88	0.95
2-4	7	165.43±28.74	17	183.60±65.78	0.35
5-9	19	222.89±59.96	22	208.23±60.63	0.44
10-14	21	384.96±164.60	21	317.39±178.33	0.20
15-19	26	444.10±159.74	43	374.18±104.26	0.05
20-24	23	392.56±95.49	25	354.66±111.59	0.21
25-29	22	390.90±95.44	23	357.00±115.30	0.29
30-39	28	345.73±98.48	28	337.98±126.77	0.79
40-49	22	376.87±95.10	28	334.90±85.86	0.10
≥50	35	344.81±99.87	49	328.96±97.96	0.47

surface. Frequency of convex superior surface was much more common in females (29%) compared to males (8.6%). Most of the females (70%) with convex superior surface were in the age group of 10–29 years.

Discussion

The size and shape of a normal pituitary gland undergoes considerable dynamic changes during lifespan and is affected by the age and gender.[9–13]So, knowing normal range of pituitary dimension is very important to identify normal from abnormal sized pituitary gland. We conducted this study with intention of establishing normal measurements of pituitary gland in Indian population.

We observed that differences in mean pituitary height and volume between males and females were highly significant, whereas difference in the pituitary length just reached statistical significance. And, there was no difference in mean pituitary width between males and females. Mean pituitary gland height in our study was 5.80 ± 1.32 mm and 5.37 ± 1.25 mm for females and males, respectively. Denk *et al*. reported mean pituitary height of 6.1 + 0.1 mm in females and 5.6 ± 0.2 mm in males respectively, which was slightly higher than mean of our population. Suzuki *et al*. reported smaller pituitary heights (5.0 ± 1.7 mm in women and 4.7 ± 1.4 mm in men) compared to our study.[13] These two studies with numerous other studies have also reported higher pituitary height in females compared to males.[7,14,15]

Mean pituitary gland height in 2 to 4-year age group was lower compared to children younger than 2 year, for both boys and girls. Earlier, Elster *et al*. and Argyropoulou *et al*. also have described gradual decrease in pituitary gland height during the first year of life.[11,12]After 5 years of age, pituitary height increased progressively in both sexes, until it reached its maximum. Maximum pituitary height was observed during second decade of life in both sexes. But, girls achieved peak pituitary height earlier (10 to 14-year age group) than boys (15 to 19-year age group). This finding can be explained on the basis of girls entering puberty little earlier than boys. Pubertal spurt in pituitary height was earlier and more robust in girls than in boys. Hayakawa *et al.*, Denk *et al.*, Suzuki *et al.* and Elster *et al.* reported peak pituitary height in second decade of life, while few authors reported maximum height of pituitary gland in the third decade of life.[3–6,9,13,16] But none of earlier studies reported any gender difference in achieving peak pituitary height.

After reaching its maximum in second decade of life, there was trend of gradual decline in pituitary height in both sexes with age. We noted that mean pituitary height increased again during fifth decade of life in females. Earlier Hayakawa *et al*., Tsunoda *et al*. and Doraiswamy *et al*. also have reported an increase in pituitary gland height in older females.[1,4,16] They attributed this phenomenon of increase in pituitary height in older females to increased activity of gonadotrophs due to loss of negative feedback by gonadal steroids. In our study, pituitary height increased marginally in males as well after 50 years of age. This observation is not reported in earlier studies. We do not know whether this increase in pituitary height in older males can be explained by similar mechanisms responsible for increase in pituitary height in older females, though phenomenon of andropause in males is not as well-established entity as menopause in females.

Changes in pituitary gland length and width did not parallel changes in pituitary height. Any spurt was not seen in either pituitary gland length or width. Differences in the mean pituitary length and width between two sexes did not follow any definitive pattern. Earlier authors have also reported poor utility of pituitary length and width in reflecting overall pituitary size.[11,13,17] This is because pituitary gland is bounded by bony structures inferiorly and laterally. Any change in the pituitary size is reflected by change in pituitary height, but not by change in length or width. This peculiar anatomy of pituitary gland makes pituitary height as simplest and reliable indicator of pituitary size.

Age- and sex-specific changes in the calculated pituitary gland volume closely paralleled changes in pituitary gland height. Pituitary volume increased progressively in first year onwards and reached its maximum during second half of second decade in both sexes. Difference in pituitary volumes

of males and females was statistically significant in the age group of 15–19 years. Han *et al*. also described progressive increase in the pituitary volume in children aged 1–19 years, using 3D volumetric MRI. He also noted spurt in the pituitary gland volume in second decade of life and maximum pituitary volume was seen in 15 to 19-year age group.[18] Takano *et al*. also have described similar trend in pituitary volume with aging.[19]

Overall, most frequently observed shape of the superior surface of pituitary gland was concave (209 subjects, 43.4%) and least common observation was convex superior surface. Only 85 (17.6%) subjects had pituitary gland with convex superior surface. Frequency of convex superior surface was much more common in females (29%) compared to males (8.6%). Most of the females (70%) with convex superior surface were in the age group of 10–29 years. Earlier studies also have reported significantly higher prevalence of pituitary gland with convex superior surface in young females.[1,15]

Mean pituitary height described by various authors are different for different populations. It may not be reasonable to use data derived from different population to use as reference value for Indian population. Based on the results of our study, we propose pituitary gland should be defined as hypoplastic or hyperplastic of its height is <2 SD or >2 SD from the mean for age-and sex-matched Indian subjects.

To the best of our knowledge, this is the largest systematically performed study to generate normative measurements of pituitary gland including subjects of all age group. We carefully excluded patients with clinical conditions, potentially affecting pituitary size. We used mid-sagittal T1-WI to measure pituitary dimensions, which is the ideal MRI sequence for the study of pituitary anatomy. Limitations of our study were few; we could not recruit sufficient number of subjects in age group of less than 5 years for both sexes, as most of them were excluded because of their illnesses. Another important limitation was subjects in our study were not healthy volunteers but patients with suspected or confirmed diseases.

Conclusion

In this study, we describe pituitary gland size and shape in 482 Indian subjects with apparently normal pituitary function. Overall, females had higher pituitary gland height and volume than males. Maximum pituitary gland height was seen in 10 to 14-year age group in females and 15 to 19-year age group in males. Maximum pituitary gland length was seen in 40 to 49-year age group in males and ≥50-year age group in females. Maximum pituitary gland width was seen during fourth decade of life in females and fifth decade of life in males. Peak pituitary gland volume was observed in 15 to 19-year age group for both sexes. Majority of subjects had either concave (43.4%) or flat (39%) superior surface of pituitary gland. Convex superior surface was significantly more frequent in females than in males. Results of our study can be used as reference values to define pituitary hypoplasia and hyperplasia for Indian subjects.

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Conflicts of interest

There are no conflicts of interest.

References

1. Doraiswamy PM, Potts JM, Axelson DA, Husain MM, Lurie SN, Na C, *et al*. MR assessment of pituitary gland morphology in healthy volunteers: Age- and gender-related differences. AJNR Am J Neurodiol 1992;13:1295-9.
2. Dietrich RB, Lis LE, Greensite FS, Pitt D. Normal MR appearance of the pituitary gland in the first 2 years of life. Am J Neuroradiol 1995;16:1413-9.
3. Kato K, Saeki N, Yamaura A. Morphological changes on MR imaging of the normal pituitary gland related to age and sex: Main emphasis on pubescent females. J Clin Neurosci 2002;9:53-6.
4. Tsunoda A, Okuda O, Sato K. MR height of the pituitary gland as a function of age and sex: Especially physiological hypertrophy in adolescence and in climacterium. Am J Neuroradiol 1997;18:551-4.
5. Elster AD, Chen MY, Williams DW 3rd, Key LL. Pituitary gland: MR imaging of physiologic hypertrophy in adolescence. Radiology 1990;174:681-5.
6. Denk CC, Onderoglu S, Ilgi S, Gurcan F. Height of normal pituitary gland on MRI: Differences between age groups and sexes. Okajimas Folia Anat Jpn 1999;76:81-7.
7. Argyropoulou M, Perignon F, Brunelle F, Brauner R, Rappaport R. Height ofnormal pituitary gland as a function of age evaluated by magnetic resonance imaging in children. Pediatr Radiol 1991;21:247-9.
8. Di Chiro G, Nelson KB. The volume of the sella turcica. AJR 1962;87:989-1008.
9. Elster AD, Sanders TG, Vines FS, Chen M. Size and shape of the pituitary gland during pregnancy and post partum: Measurement with MR imaging. Radiology 1991;181:531-5.
10. Gonzales G, Elizondo G, Saldivar D. Pituitary gland growth during normal pregnancy: An in-vivo study using magnetic resonance imaging. Am J Med 1988;85:217-20.
11. Cox TD, Elster AD. Normal pituitary gland: Changes in shape, size, and signal intensity during the first year of life at MR imaging. Radiology 1991;179:721-4.
12. Argyropoulou M, Perignon F, Brunelle F, Brauner R, Rappaport R. Height of normal pituitary gland as a function of age evaluated by magnetic resonance imaging in children. Pediatr Radiol 1991;21:247-9.
13. Suzuki M, Takashima T, Kadoya M, Konishi H, Kameyama T, Yoshikawa J, et al. Height of normal pituitary gland on MR imaging: Age and sex differentiation. J comput assist tomogr 1990;14:36-9.
14. Fujisawa I, Asato R, Nishimura K, Togashi K, Itoh K, Nakano Y, *et al*. Anterior and posterior lobes of the pituitary gland: Assessment by 1.5T MR imaging. J Comput Assist Tomogr 1987;11:214-20.
15. Elster AD, Chen MYM, Williams DW, Key LL. Pituitary gland: MR imaging of physiologic hypertrophy in adolescence. Radiology 1990;174:681-5.
16. Hayakawa K, Konishi Y, Matsuda T, Kuriyama M, Konishi K, Yamashita, K *et al*. Development and aging of brain midline structures: Assessment with MR imaging. Radiology 1989;172:171-7.
17. Lurie SN, Doraiswamy PM, Husain MM, Boyko OB, Ellinwood EH Jr, Figiel GS, et al. In vivo assessment of pituitary gland volume with magnetic resonance imaging: The effect of age. J Clin Endocrinol Metab 1990;71:505-8.
18. Han X, Xiu J, Huang Z, Zhang J, Zhang Z, Dong Y, *et al*. Three dimensional magnetic resonance volumetry of the pituitary gland is effective in detecting short stature in children. Exp Ther Med 2014;8:551-6.
19. Takano K, Utsunomiya H, Ono H, Ohfu M, Okazaki M. Normal development of the pituitary gland: Assessment with three dimensional MR volumetry. Am J Neuroradiol 1999;20:312-5.