CASE REPORT

Evaluation of Size of Normal Adult Pituitary Gland on Magnetic Resonance Imaging

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ABSTRACT

Background: The size of pituitary gland differs with age, gender, or stage of life. The pituitary gland may malfunction, and result in hyper-functioning of the gland or hypo-functioning of the gland. Whether the size of an organ is normal or abnormal is one of the signs of a disease. In case of pituitary gland, reliable data on the normal range of size and volume lacks, especially in Indian population. A hospital based retrospective study at a tertiary care centre in India was done and cases were taken up for imaging of pituitary gland, to analyse the size of normal pituitary gland in Indian adult males and females on Magnetic Resonance Imaging (MRI). On a 1.5 Tesla MRI machine; curvilinear length, linear length, width, height, and volume of the anterior pituitary gland were taken, and descriptive and inferential statistical analysis were carried out.

Results: Pituitary height is the most reliable and consistent individual morphometric parameter for assessing pituitary. Females have larger pituitary size and volume than males across all age groups, although this difference was most marked in 18-25 years.

Conclusion: The difference of pituitary size across different age groups in males and females can further help in formulating age group specific normograms for Indian adults. This study can form the base for further studies that include a larger number of healthy volunteers.

Keywords: MR Morphometry; Normogram; Pituitary gland; Size.

INTRODUCTION

As most pathologies result in increase or decrease in the size of the pituitary gland, imaging plays a critical role in determining the normal morphological range of pituitary gland and differentiating normal from abnormal. This becomes even more important in cases with borderline abnormalities or inconclusive hormonal parameters.

Pituitary gland can be evaluated directly and indirectly using radiograph, CT and MRI of the head. While radiograph gives an indirect idea about pituitary gland through sella turcica, CT shows both bony and soft tissue structures.

MRI is the modality of investigation that has unique advantage of non-invasive evaluation of pituitary gland without exposure to ionizing radiation. With the advent of better and faster hardware as well as software in MR imaging, it is now possible to measure pituitary gland accurately.

By this study, we have established age and sex based pituitary normogram to establish its normal range for Indian population.

METHODS

The present study was carried out as a cross sectional study in a tertiary care teaching hospital on Indian population for a period of 2 years. Purposive sampling technique was followed to recruit eligible study participants. All patients in the relevant age group who underwent MRI brain for non-pituitary disease and subsequently found to have normal study were included in the study.

Inclusion criteria:

- Patients between the ages of 18-45yrs undergoing MRI Brain for a non-pituitary disease.

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- MRI brain is normal.
- Informed written consent has been given by the patient.

Exclusion criteria:

- Pregnant females
- Patient contraindications for MRI such as ferro magnetic, electromagnetic implants.
- Known pituitary disease.
- Empty sella.

After taking a written informed consent, MRI of the brain was performed using Siemens 1.5 T Magnetom Avanto scanner. For T1 MPR sequence, scan parameters were kept as- TE: 4.3, TR: 1160, TI: 600, FOV: 236*270, SL- 0.9mm BW- 180. Measurements were recorded as per the proforma.

Technique:

T1 MPR images were further studied for a detailed evaluation of pituitarygland. Mid sagittal images were analysed to calculate linear and curvilinear length, while the coronal image at pituitary stalk was used to calculate the width and height of the gland.

Pituitary volume was calculated using the formula $V = 0.52*L*W*H$ {V= volume, L= length, W= width, H= height. This factor of 0.52 was obtained from the sphere value equation coefficient and cubic volume calculation i.e $(4/3\pi)(r3)/(2r)3 = 3.1416/6 = 0.52$}. To standardise the measurement length was taken at mid sagittal position and width and height were taken at the level of pituitary stalk in the coronal plane.

Statistical Analysis

Descriptive and inferential statistical analysis has been carried out in this study. Results on continuous measurements are presented on Mean, +/- SD (Min-Max) and results on categorical measurement are presented in number (%).

The sample size was determined using Cochran's formula, and was found out to be 145 considering estimated proportion to be 90% calculated based on frequency.

The desired level of precision is 5%, and significance is assessed at 5% level of significance.

A linear regression model was constructed for finding important factors. The model was built assuming sex, age and curvilinear length to be a prime predictor of the response variable pituitary volume:

The P-value of sex and age was found to be 0.059 and 0.608 and effect of CL (Curvilinear Length) on pituitary volume can be neglected because of $P < 0.0001$. R square value of 0.917, which shows that the model is moderately able to capture the variance.

Statistical Software: The statistical software, namely Python 3.6, analysed on Jupyter notebook. In the given table, the p values for curvilinear length, Sex and Age are 0.000, 0.059 and 0.608, which shows the decreasing significance on the predictor variable.

In this study, p-value of 0.000 implies that the effect of curvilinear length on volume is statistically significant (using $p < 0.05$ as a rejection rule) than the sex and age respectively.

RESULTS:

Table 1: Distribution of participants by age group and gender

	Males	Females
Age group (in yrs.)	Frequency	Frequency
18-25	36	11
26-35	32	16
36-45	31	20

Overall participants involve the majority of the male population in the age group 18-25 followed by rest of the age groups. For females, the majority of the sample is in the age group of 36-45 followed by age group 26-35 and least in 18-25

Table 2: Average pituitary volume of study participants (n=146)

Gender	Volume (cm^3)
Male	0.50
Female	0.57

Table 3: Average height and curvilinear length of pituitary of study participants

Gender	Average Height(cm)	Average CL(cm)
Male	0.687	1.568
Female	0.694	1.607

Table 4: Average gender-wise volume of pituitary gland.

	Males		Females	
Age group (in yrs.)	Mean (in cm^3)	SD (in cm^3)	Mean (in cm^3)	SD (in cm^3)
18-25	0.5204	0.1629	0.6516	0.1011
26-35	0.5208	0.1653	0.6236	0.0993
36-45	0.4655	0.1244	0.4765	0.1325

Table 5: Average age wise curvilinear length of pituitary gland.

	Males		Females	
Age group(in yrs.)	Mean (in cm)	SD (in cm)	Mean (in cm)	SD (in cm)
18-25	1.5943	0.1934	1.6711	0.1609
26-35	1.5363	0.1456	1.6416	0.1406
35-45	1.5784	0.1924	1.5389	0.1768

No significant difference in mean curvilinear length of the male in the different age group from 18 to 45. In female mean curvilinear length drops by 0.10 cm from the age group of 18-25 to 36-45.

Table 6: Average height of pituitary gland by age and gender

	Males		Females	
Age group (in yrs.)	Mean (in cm)	SD (in cm)	Mean (in cm)	SD (in cm)
18-25	0.6848	0.1918	0.7332	0.0803
26-35	0.7748	0.3064	0.7447	0.2149
36-45	0.6161	0.1943	0.6168	0.2358

Mean height of pituitary gland in males is seen highest in the age group of 26-35 years followed by 18-25 years and lowest in the age group of 36-45 years. A similar trend is there for females, but there is a minute difference of mean height in the age group of 26-35 years and 18-25 years and a significant reduction in the age group of 36-45 years.

Table 7: Average width of pituitary gland by age and gender

	Males		Females	
Age group (in yrs.)	Mean (in cm)	SD (in cm)	Mean (in cm)	SD (in cm)
18-25	1.2683	0.2509	1.5292	0.0647
26-35	1.2131	0.3446	1.3893	0.2713
36-45	1.2917	0.2208	1.2953	0.2671

In Male mean width of the pituitary gland is highest in the age group of 36-45 followed by 18-25 and least in 26-35. Where as in average female width is seen highest in the age group of 18-25 and keeps reducing as we move up the age.

Table 8: Average AP length of pituitary gland by age group and gender

	Males		Females	
Age group (in yrs.)	Mean (in cm)	SD (in cm)	Mean (in cm)	SD (in cm)
18-25	1.1626	0.0868	1.1117	0.1106
26-35	1.1426	0.1145	1.2007	0.0940
36-45	1.1410	0.1118	1.1893	0.1313

In male mean AP, the length is seen highest in the age group of 18-25, and not much difference in rest of the study participants whereas in females mean AP length is seen highest in the age group of 26-35 followed by 36-45 and least in the age group of 18-25.

Table 9: Statistical analyses for age group of 18-25

Parameter	Gender	Mean ± SD	Minimum	Maximum	95% C.I	
					Lower	Upper
AP length	Male	1.1626 ± 0.0868	0.99	1.42	0.9925	1.3327
	Female	1.1117± 0.1106	0.91	1.32	0.8950	1.3285
Curvilinear Length	Male	1.5943± 0.1934	1.08	2.06	1.2152	1.9734
	Female	1.6711± 0.1609	1.44	2.02	1.3557	1.9864
Width	Male	1.2683± 0.2509	0.32	1.64	0.7765	1.7600
	Female	1.5292 ± 0.0647	1.44	1.64	1.4024	1.6560
Height	Male	0.6848± 0.1918	0.35	1.27	1.0607	0.3088
	Female	0.7332± 0.0803	0.59	0.91	0.5758	0.8906
Volume	Male	0.5204± 0.1629	0.2236	0.8194	0.2011	0.8396
	Female	0.6516± 0.1011	0.5472	0.9176	0.4534	0.8497

The last column indicates the lower and upper boundary of the respective parameters with 95% confidence for the selected sample of volunteers.

The last column indicates the lower and upper boundary

Table 10: Shows the summary statistics of all the parameters considered based on gender for the age group of 26-35.

Parameter	Gender	Mean ± SD	Minimum	Maximum	95% C.I	
					Lower	Upper
AP length	Male	1.1426± 0.1145	0.82	1.45	0.9182	1.3670
	Female	1.2007± 0.0940	1.02	1.39	1.0165	1.3849
Curvilinear Length	Male	1.5363 ±0.1456	1.09	1.84	1.2510	1.8217
	Female	1.6416± 0.1406	1.37	1.88	1.3660	1.9172
Width	Male	1.2131± 0.3445	0.29	1.65	0.5379	1.8883
	Female	1.3893 ±0.2713	0.65	1.76	0.8575	1.9210
Height	Male	0.7748± 0.3064	0.40	1.55	0.1742	1.3753
	Female	0.7447± 0.2149	0.54	1.50	0.3235	1.1659
Volume	Male	0.5209±06.1653	0.2042	0.7899	0.1969	0.8449
	Female	0.6236± 0.0993	0.4524	0.8405	0.4290	0.8182

The last column indicates the lower and upper boundary of the respective parameters with 95% confidence for the selected sample of volunteers.

Table 11: Shows the summary statistics of all the parameters considered based on gender for the age group of 36-45

Parameter	Gender	Mean ±SD	Minimum	Maximum	95% C.I	
					Lower	Upper
AP length	Male	1.1410±0.1118	0.91	1.35	0.9218	1.3601
	Female	1.1893±0.1313	1.05	1.67	0.9319	1.4466
Curvilinear Length	Male	1.5784±0.1924	1.17	2.09	1.2013	1.9555
	Female	1.5389± .1768	1.05	1.89	1.1923	1.8854
Width	Male	1.2917±0.2208	0.46	1.69	0.8589	1.7244
	Female	1.2953±0.2671	0.51	1.72	0.7717	0.8188
Height	Male	0.6161±0.1943	0.38	1.5	0.2352	0.9961
	Female	0.6168±0.2358	0.38	1.5	0.1546	1.0789
Volume	Male	0.4655±0.1244	0.1822	0.6830	0.2216	0.7093
	Female	0.4765±0.1325	0.2694	0.7532	0.2168	0.7362

of the respective parameters with 95% confidence for the selected sample of volunteers.

DISCUSSION

This study was carried out as a cross sectional study among patients who underwent MRI of the brain for any non-pituitary abnormality and subsequently found to have normal study on MRI.

In current practice, assessing pituitary size and volume is mostly a subjective attempt with lack of objectivity due to lack of sufficient data and studies on the Indian population.

Development of normogram of pituitary size and volume in young Indian adults with the help of MRI will be beneficial for the identification of abnormal pituitary size in borderline cases and their management.

During the lifespan of an individual, the size and shape of the normal pituitary gland is dynamic. Age and gender (male and female) plays a pivotal role in the same. It is important to know the normal range of pituitary dimension to distinguish between the normal and abnormal size of the pituitary gland. Hence this study was conducted to establish pituitary volume and size of normal Indian subjects between the age of 18-45 years.

Herein, we present a systematic comparison of our study results with previous similar ones.

Bughio et al.[2] have taken a sample of 290 subjects (152 males, 138 females) in 10 to 70 years age group and have concluded that females have significantly greater pituitary width and volume compared to males. Maximum height of the gland is achieved in 2nd decade of life. Volume of the gland is maximum in the third decade of life. Mean volume in their study is 0.45 ± 0.115 cm^3. Our sample size is approximately half of that of Bughio et al. (99 males, 47 females). Mean volume in our study has been calculated as 0.503 ± 0.153 cc for male and 0.568 ± 0.138 cc for females. The statistical figure is largely comparable. The difference in volumes noted can be on account of the difference in the age group of samples.

Castillo has referred to Amar AP, Weiss MH and stated that the gland grows rapidly in the first two decades of life and after the fourth decade of life the gland loses weight. The changes are more prominent in males. It is heavier for females by approximately 20%. Normal Size of the gland is approximately 10mm in length, 5 to 10 mm in height and 10-15 mm in width. For our study, the average length is 11.67 ± 1.09 mm, average height is 6.91 ± 2.31 mm, and the average width is 12.98 ± 2.73 mm. As can be seen, our values are consistent with what Castillo et al.3 have quoted.

Rahman, Sharif et al.[4] have taken a sample of 100 subjects in the age group of 14 to 82 (Mean age 40) and observed that pituitary height and volume correlate negatively with increasing age. They could not find any statistically significant difference between the height and volume of male and female. Mean pituitary heights were 6.22 ± 1.6 mm for males and 6.42 ± 1.57 mm for females. They have reported higher mean volume in males (332.1 ± 146.8 mm3) compared to females 324.1 ± 130.2 mm^3. However, they have concluded that the difference is not statistically significant. This may be because of the lower sample size spread across a vast age group.

Table 12: Compares the measurements of the present study with previous similar studies

Parameters	Rahman, Sharif et al.	Ramalingaiah, Kaushal et al[5]	Present study
Height (M)	6.22 ± 1.6 mm	5.82 ± 1.54 mm	6.92 ± 2.42 mm
Height (F)	6.42 ± 1.57 mm	6.03 ± 1.63 mm	6.88 ± 2.08 mm
Volume (M)	0.332 ± 0.147 cc	0.40 ± 0.16 cc	0.503 ± 0.153 cc
Volume (F)	0.324 ± 0.130 cc	0.42 ± 0.16 cc	0.568 ± 0.138 cc

Ramalingaiah and Kaushal[5] have conducted a study on 200 samples between the age group of 10 to 19 and have reported mean volume as 0.42 ± 0.16 cc and 0.40 ± 0.16 cc for females and males respectively. Females have a slightly larger pituitary gland, but the difference was not statistically significant. For their sample, the volume has shown a gradual increase with age, which is expected for the age group.

Naik Reddy et al.[6] have taken samples for an age group of 10 to 19 and reported volume as 400 ± 150 mm3 in males and 430 ± 170 in females. Females have slightly larger glands, but the difference is not statistically significant. For the given sample, there was an increase in volume with age.

Sanjay et al.[7] have observed (sample 120 females of age 20 to 60 years) that mean height of Pituitary Gland is 6.27 mm ± 0.56, Mean length 9.10mm ± 0.78, Mean width 11.22 mm ± 0.82. It was seen that the size of the gland changes with age. Height decreased significantly with age. However, a mild increase in the height was noted in the age group of 40-49 yrs. Maximum width was noted in the 3rd decade. Length increased up to 40 years and later decreased.

Values reported in our study for the age group of 18-45 years in females is consistent with those reported by Sanjay et al.

Table 13: Shows another comparison of the present study with a previous similar study done by Sanjay et al. for females.

Parameters	Sanjay et al	Present Study
Mean Height	6.27 ± 0.56 mm	6.88 ± 2.08 mm
Mean Length	9.10 ± 0.78 mm	11.75 ± 1.18 mm
Mean width	11.22 ± 0.82 mm	13.82 ± 2.51 mm

As per multiple studies, we have observed that length and width of pituitary gland does not play a significant role in the determination of actual pituitary size or volume. Any change in the pituitary size is influenced by the change in pituitary height. Change in length or width doesn't alter the pituitary size. This peculiar anatomy of pituitary gland makes pituitary height as the simplest and most reliable

indicator of pituitary size. Age and sex specific changes in the calculated pituitary gland volume closely paralleled changes in pituitary gland height. The pituitary volume progressively increased in the first year onwards and reached its maximum dimension during the second half of the second decade in both sexes. The difference in pituitary volumes of males and females was statistically significant in the age group of 15–19 years. Han et al. also described a progressive increase in the pituitary volume in children aged 1–19 years. This was done using 3D volumetric MRI. He also noted spurt in the pituitary gland volume in the second decade of life, and maximum pituitary volume was seen in 15 to 19 year age group. Takano et al. also have described a similar trend in pituitary volume with aging8.

Table 14: Comparison of the present study with other previous studies (Volume)

Parameters	Singh, Kandasamy et al.	Present study
Average Pituitary volume(M/F)	0.31/0.35 cc	0.50/0.57cc
Average Pituitary length(M/F)	0.90/0.93 cm	1.15/1.18 cm
Average Pituitary height(M/F)	0.54/0.58 cm	0.69/0.69 cm
Average Pituitary width(M/F)	0.12/0.13 cm	1.26/1.38 cm

As noted, that Arun KC Singh et al.9 reported that difference of the mean pituitary height and volume between males and females, which were highly significant.

Table 15: Comparison of pituitary height in our study with other studies (Height)

Mean Height (mm)	Arun K C Singh	Denk et al	Suzuki et al	Present Study
Male	5.37 ± 1.25	5.6 ± 0.2	4.7 ± 1.4	6.92 ± 2.26
Female	5.80 ± 1.32	6.1 ± 0.1	5.0 ± 1.7	6.67 ± 1.71

Above studies with numerous other studies have also reported higher pituitary height in females compared to males.

Hayakawa et al., Denk et al., Suzuki et al. and Elster et al. reported peak pituitary height in the second decade of life, while few authors reported maximum height of pituitary gland in the third decade of life. But

none of the earlier studies reported any gender difference in achieving peak pituitary height. After reaching its maximum in the second decade of life, a gradual decline in pituitary height in both sexes with age was noted.

Since our study considers the second, third and fourth decade of life specifically, we observed peak pituitary height was specific in the age group of 26-35 in males as well as females.

Earlier Tsunoda et al., Hayakawa et al., and Doraiswamy et al. also have reported an increase in pituitary gland height in older females. They attributed this phenomenon of an increase in pituitary height in older females to increased activity of gonadotropins due to loss of negative feedback by gonadal steroids. In our study, pituitary height decreased marginally in males as well as females in mid-thirties. 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 the increase in pituitary height in older females, though the phenomenon of andropause in males is not as well established an entity as menopause in females.

In our study, we have included 146 cases of age groups 18-45. Length, curvilinear length, width, height and volume were calculated considering pituitary as irregular ellipsoid structure.

Our study faces limitation on count of over representation of male candidates (99 males and 47 females) and the fact that we have considered only three age groups, i.e., 18-25; 26-35 and 36-45 thereby leaving no scope of comparison outside these age brackets.

We carefully excluded patients with clinical conditions, potentially affecting the pituitary size. Besides, we have also excluded patients who were found to have partially empty Sella after the MRI scan. We used mid sagittal T1W MPR to measure pituitary dimensions, which is the ideal MRI sequence for the study of pituitary anatomy.

CONCLUSION

The present study conducted over 146 participants with a normal study of MRI brain and no known pituitary pathology led to the following important conclusions:

Females, in general, have larger pituitary size and volume than males across all age groups, although this difference was most marked in 18-25years.

Pituitary height was the most reliable and consistent individual morphometric parameter for assessing pituitary.

Width of the pituitary gland, when measured in the coronal plane, showed an unusual peak in males at 36-45 years. This needs further investigation through larger studies for reasons and its possible clinical implications.

There was an almost consistent trend of decline in pituitary morphometric parameters after the second half of the 3rd decade of life.

Findings of the present study matched with most of the previous similar studies done in the same age group.

Normal values provided in this study for adult Indian population can act as a database to identify the normal from diseased subjects. This will also help to appreciate the difference in pituitary morphology between adult males and females.

The difference of pituitary size across different age groups in males and females can further help in formulating age group specific nomograms for Indian adults. This study can form the base for further studies that include a larger number of healthy volunteers.

Abbreviations: Not applicable

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