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NORMATIVE ASSESSMENT OF PITUITARY MORPHOLOGY IN MAGNETIC RESONANCE IMAGING (MRI)

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Abstract:

Background: There are relatively fewer studies describing the morphometry of the pituitary gland for the Indian population. These studies also show a wide range of variation in their normal range of measurements. Hence there is no definitive yardstick for the normal dimensions of the pituitary gland. **Aims and objectives:** To study and establish an age-based normogram for the dimensions of the pituitary gland in males and females for Indian population. **Material and methods:** This descriptive and collaborative study was performed between June 2018 and June 2020. Patients of all age groups referred for Magnetic resonance imaging (MRI) Brain were included. Patients with known pituitary pathology were excluded. MRI was done using Siemens 1.5 Tesla MAGNETOM ESSENZA MRI scanner, Erlangen Germany. The anteroposterior (AP) diameter, transverse diameter and craniocaudal measurements of the pituitary gland were measured. Student unpaired t-test, ANOVA and Cohen's kappa value for inter-observer agreement were used. **Results:** The length, width, height and volume of the pituitary gland showed significant variations with age. The volume of the pituitary gland is a better marker of pituitary activity. Volume of the pituitary gland was significantly higher in females compared to males, specifically in the second and third decades. We also observed two peaks in the volume of the pituitary gland; the first noted in 10-20 years age group in both males and females corresponding to puberty and increased hormonal activity and a small second peak in 50-60 years age group. **Conclusion:** This study provides measurements of pituitary gland and its variations based on age and sex. We also observed two peaks in the volume of the pituitary gland, one in 2nd decade and another in 5th decade, in both males and females.

Keywords: Magnetic resonance imaging, pituitary gland, height, length, width, volume, normogram, morphometry

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1. Introduction

Pituitary gland is known to show a wide range of variation in its morphology with age and sex. A methodical approach to the pituitary region is very important because findings can be exceedingly subtle. Variations seen in size and shape of pituitary gland reflect the changes in complex hormonal physiology of the gland. Subtle abnormalities like physiological hypertrophy, increased lobulated margins, inflammation can be challenging to diagnose due to insufficient data. A reference measurement of the normal pituitary gland for various age ranges can be particularly beneficial in diagnosing such cases.

For comprehensive and accurate assessment of pituitary gland, it is therefore imperative to know its normal anatomy along with the physiological variations in its shape and size in diverse age groups in both genders. Magnetic Resonance Imaging (MRI) is considered the mainstay for imaging of intracranial soft –tissue structures and is widely regarded as imaging of choice for the pituitary gland as well. T1 weighted sequence is primarily used for evaluation of normal morphology and in order to minimize error, it needs to be performed in both the sagittal and coronal planes for accurate measurement of pituitary size.

Various studies done in this field validate the fact that the normal pituitary morphology tends to show a wide range of variation in its dimensions. These studies done previously have been of limited use due to a narrow age group as sample population, topographical variations and other factors rendering it difficult to form a common consensus regarding normal pituitary measurements in Indian population. The purpose of this article is to compensate for the lack of quantity of such studies in the Indian population and gather sufficient amount of data to more efficiently demarcate normal from abnormal dimensions of the pituitary gland.

Aims and objectives: This study aims to provide the reference values for a normal pituitary gland and give quantitative data regarding normal range for pituitary gland size and study the variations in the dimensions of pituitary gland with respect to age and gender.

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2. Material and Methods

MRI was done using Siemens 1.5 T MAGNETOM ESSENZA MRI scanner. Our study incorporated the use of mid-sagittal T1 section for measurement of height and length of pituitary gland, mid sagittal section being considered where anterior, posterior lobes are visualized in same slice as the pituitary stalk. T2 coronal section was used to assess the width [Fig.1].

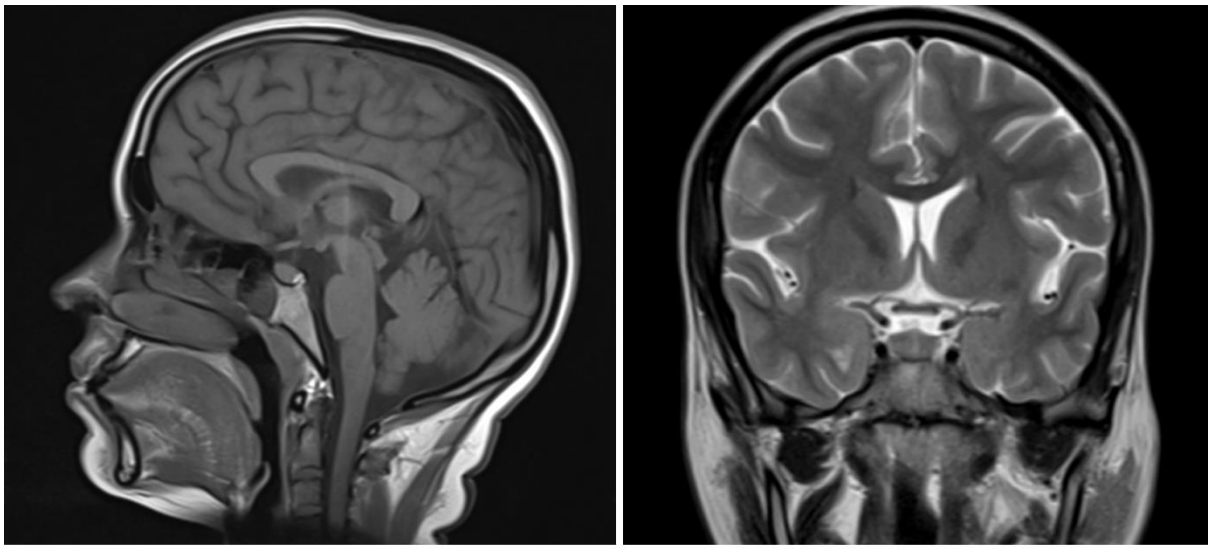

Figure 1: (A) T1 sagittal image used to measure height and length of the pituitary gland **(B)** T2 coronal image was used to measure width of the pituitary gland

The following technical specifications were used for the measurements.

- Width of the pituitary gland was measured as its maximum transverse extent in T2 coronal section.
- Length of the pituitary gland was measured as maximum anteroposterior diameter in mid sagittal section.
- Height of the pituitary gland was measured as its maximum cranio-caudal extent in T1 mid sagittal section.
- Volume of the pituitary gland was measured using the formula = [length x width x height x 0.52].

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Inclusion criteria: Patients of all age groups referred for MRI Brain.

Exclusion criteria:

1. Pathologies affecting pituitary- space occupying lesion/ increased intracranial pressure etc.
2. Patient with history of pituitary disease.
3. Patients with history of radiation/ surgery/ psychiatric illness/ anti-psychotic drugs.
4. Women of reproductive age who are currently pregnant or lactating or stopped lactating in the last 6 months of performing the MRI were excluded from the study as the measurements obtained from these subjects could skew the distribution of values.

Inter-observer variability

The study measurements were conducted by five independent investigators trained in interpreting MRI of brain. All the five investigators were blinded to the age and gender of the study population. Inter-observer agreement analysis was performed using Cohen's kappa value. For the measurements of the height and width of the pituitary gland the Cohen's kappa value was 0.94 suggesting almost perfect agreement. For the measurement of the length of the pituitary gland the Cohen's kappa value was 0.87, again suggesting almost perfect agreement. Minor discrepancies in the values obtained were averaged out of the five readings and the standard deviation of the five measurements for any given single-data-point was always less than ± 0.01 mm.

Statistical analysis

Student unpaired t-test was used to study the length, height and width of the pituitary gland in males and females. ANOVA was used to assess the dimensions of the pituitary gland and to study the relationship with age and gender. Cohen's kappa value was used to assess the inter-observer agreement in the obtained values.

Ethical consideration:

The study has been approved by the Institute Research Board and the Human Ethics Committee. As it is an image-based study with anonymization of patient data, a waiver of informed consent form was obtained.

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3. Results

The mean pituitary height & volume in our study group was found to be 5.36mm and 298cc respectively. The *p*-value for height, length, width and volume between age groups was less than 0.05 which was statistically significant in both males and females. P-value was 0.00000 (the least) and is the most significant for volume – thus we can infer that volume is a better marker of pituitary activity compared to pituitary height. ANOVA test was used for the above statistical evaluation. The *p*-value for height, length, width and volume between males and females was also less than 0.05 (statistically significant). It was evaluated using unpaired t-test.

A peak was noted in 10-20 years age group in both males and females which corresponded to puberty and increased hormonal activity. A gradual decline in pituitary dimensions was noted after the second decade. A small second peak was noted in 50-60 years age group in both sexes. Volume of pituitary was significantly higher in females compared to males, which was substantial in the second and third decades (menarche and lactation) and marginal in the rest of the age groups.

In Table 1 & Table 2 we have tabulated mean and standard deviation for height, length, width and volume of pituitary in both males and females, which can used as a standard reference for its evaluation. Graphical illustration of normative values of height (cranio-caudal diameter), length (antero-posterior diameter), width (transverse diameter) and volume are shown in Figures 2, 3, 4 and 5 respectively. These graphs help better understand the variations of the above values with age.

Table 1: Dimensions of the pituitary gland in males of different age groups

Age group	Pituitary height (mm) (mean ± SD)	Pituitary length (mm) (mean ± SD)	Pituitary width (mm) (mean ± SD)	Pituitary volume (cc) (mean ± SD)
0-10 years	4.49 ± 0.62	7.12 ± 0.76	9.78 ± 1.53	164.17 ± 41.13
11-20 years	5.49 ± 0.82	8.95 ± 1.31	11.14 ± 1.49	318.86 ± 66.01
21-30 years	5.44 ± 0.98	9.68 ± 1.13	11.65 ± 1.69	305.71 ± 97.27
31-40 years	5.41 ± 1.13	9.53 ± 1.21	10.72 ± 1.56	242.93 ± 85.39
41-50 years	5.24 ± 0.83	9.69 ± 1.28	10.36 ± 1.81	267.46 ± 64.91
51-60 years	5.27 ± 1.18	9.47 ± 1.14	10.47 ± 1.84	275.51 ± 104.43

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61-70 years	4.59 ± 1.14	9.29 ± 1.21	10.55 ± 2.02	239.44 ± 71.30
71-80 years	3.86 ± 0.77	8.73 ± 1.38	9.00 ± 1.05	169.54 ± 70.12

** SD – standard deviation*

Table 2: Dimensions of the pituitary gland in females of different age groups

Age group	**Pituitary height (mm) (mean ± SD)**	**Pituitary length (mm) (mean ± SD)**	**Pituitary width (mm) (mean ± SD)**	**Pituitary volume (cc) (mean ± SD)**
0-10 years	4.65 ± 0.48	7.92 ± 0.65	9.43 ± 1.41	180.81 ± 33.13
11-20 years	6.75 ± 1.13	9.91 ± 1.08	11.99 ± 1.45	431.17 ± 108.08
21-30 years	6.05 ± 0.78	10.01 ± 1.02	12.04 ± 1.85	347.79 ± 54.07
31-40 years	5.55 ± 1.22	9.97 ± 0.91	11.08 ± 1.5	301.32 ± 54.24
41-50 years	5.52 ± 1.1	10.23 ± 1.2	11.31 ± 1.91	249.35 ± 65.68
51-60 years	5.07 ± 0.89	9.76 ± 1.38	10.13 ± 1.74	283.61 ± 55.56
61-70 years	4.76 ± 0.88	9.81 ± 1.41	9.86 ± 1.78	193.13 ± 47.12
71-80 years	3.61 ± 0.65	9.12 ± 1.21	10.78 ± 2.05	186.36 ± 64.05

** SD – standard deviation*

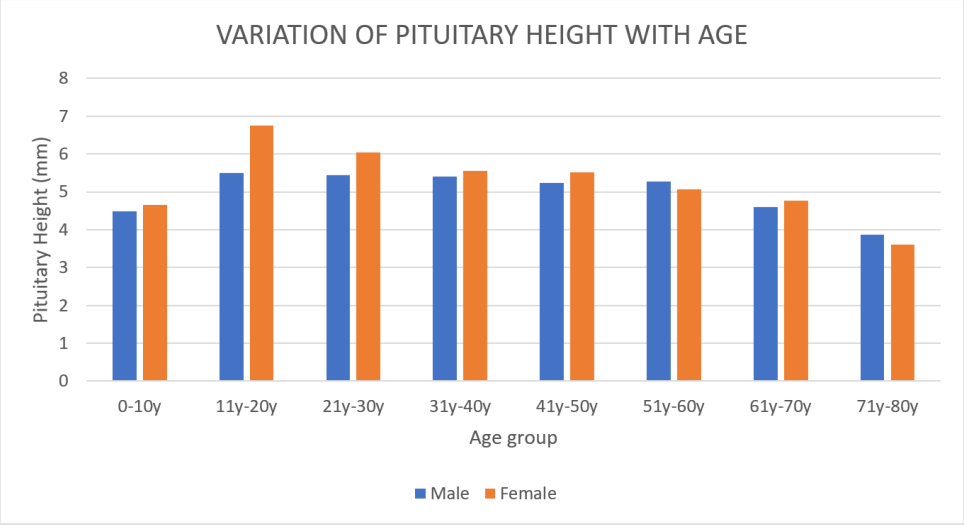

Figure 2: Graphical illustration of physiologic variations in pituitary height of males and females with age.

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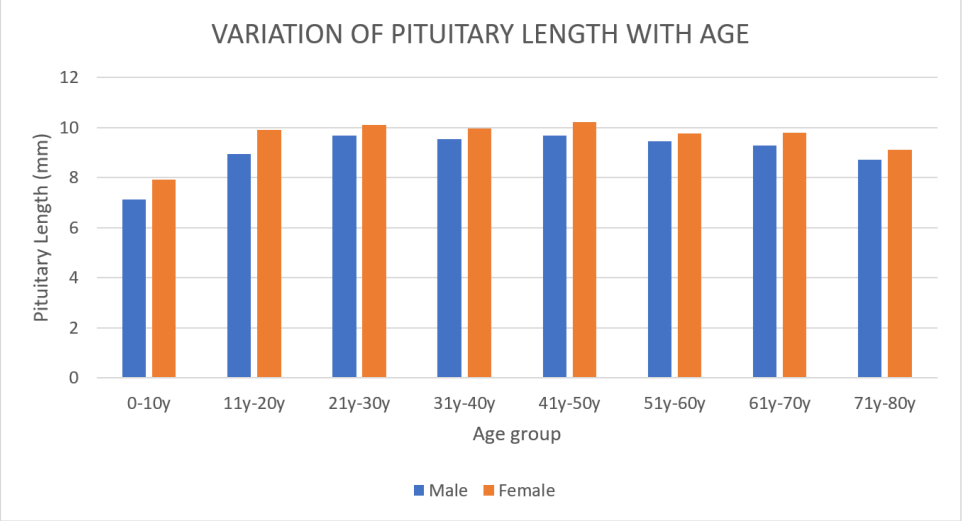

Figure 3: Graphical illustration of physiologic variations in pituitary length of males and females with age.

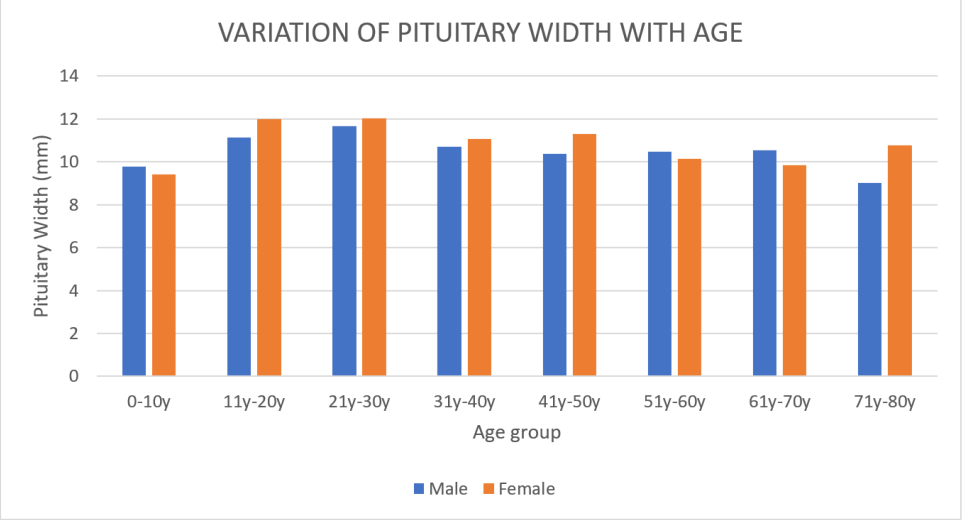

Figure 4: Graphical illustration of physiologic variations in pituitary width of males and females with age.

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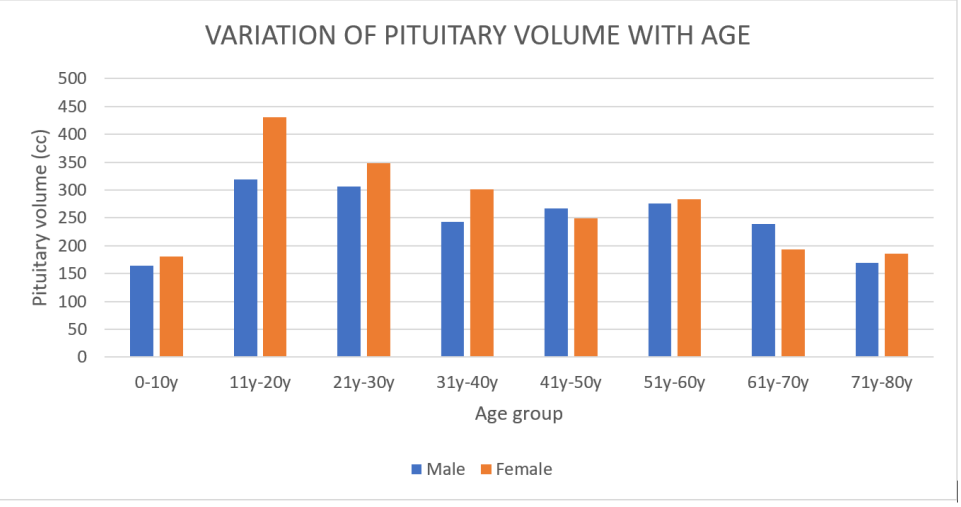

Figure 5: Graphical illustration of physiologic variations in pituitary volume of males and females with age.

Discussion:

Pituitary gland plays a significant role in normal physical growth, development and metabolism. It is located in a bony concavity of sphenoid bone called sella turcica and surrounded by the parasellar region containing sphenoid sinus, cavernous sinuses and other important structures [1]. It is composed of two lobes called adenohypophysis (anterior lobe) and neurohypophysis (posterior lobe) based on their function [2, 3].

The anterior lobe constitutes approximately three fourth of volume of the gland. It consists of pars tuberalis, pars intermedia and pars distalis. Its blood supply is by hypophyseal portal system. The hormones secreted by adenohypophysis include growth hormone (GH), adrenocorticotropic hormone (ACTH), prolactin (PRL), thyroid stimulating hormone (TSH), luteinizing hormone (LH), and melanocyte-stimulating hormone (MSH) [4,5]. Rest of the volume of the gland is formed by neurohypophysis (posterior lobe, infundibular stalk, supraoptic, and paraventricular hypothalamic nuclei) which acts as a storage organ for oxytocin and vasopressin, the hormones synthesised in hypothalamus and transported by hypothalamo-hypophyseal tract.

MRI is the mainstay for imaging of pituitary gland. Adenohypophysis appears isointense to cerebral cortex on T1W and T2W images while neurosecretory vesicles lead to appearance of neurohypophysis as bright spot on T1WI [6, 7, 8]. Pituitary shape can also play an important role in its evaluation. A few studies have stated a way of evaluating pituitary size by examining its superior border. It can be convex, flat or concave. A convex border can be observed in puberty or lactating period and is suggestive of increased pituitary activity

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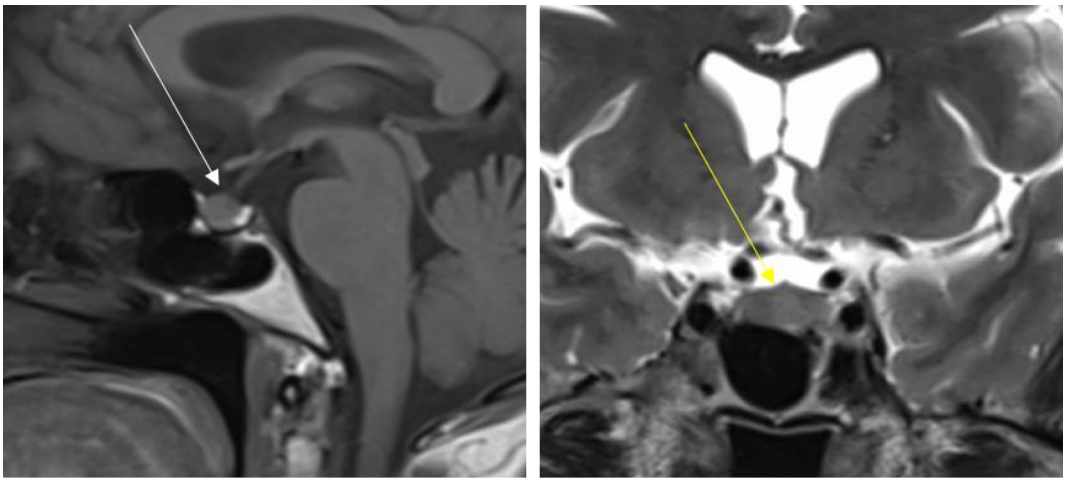
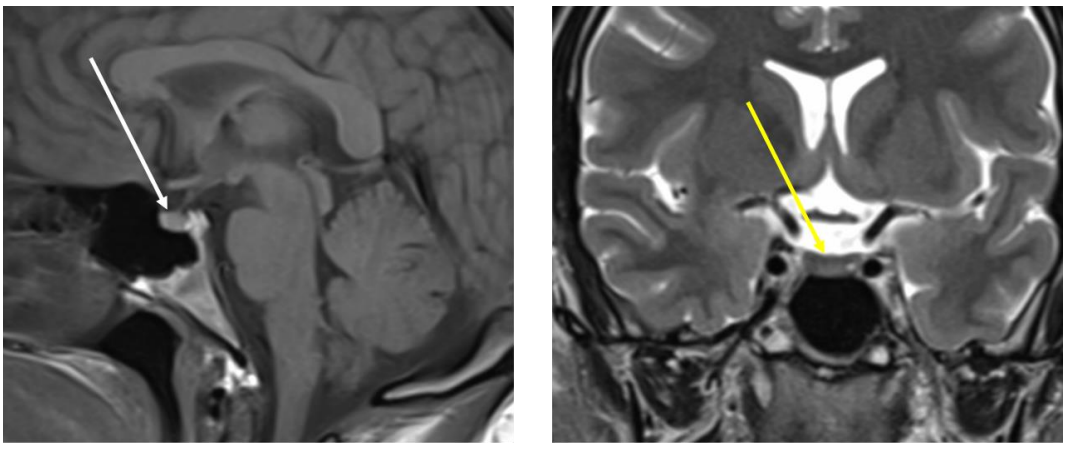
[Fig.6]. A flat upper border is usually seen in fourth and fifth decades when the pituitary activity is neither peaking nor has it bottomed out [Fig.7] and flat upper border is the most commonly seen type in general population. A concave upper border is usually seen in the later age group i.e. post sixth decade when there is significant fall in pituitary activity [Fig.8].



A B

Figure 6: (A) T1 mid sagittal and **(B)** T2 coronal sections of brain in a 19year old female showing a convex upper border (white arrow in A and yellow arrow in B).



A B

Figure 7: (A) T1 mid sagittal and **(B)** T2 coronal sections of brain in a 38year old female showing a flat upper border (white arrow in A and yellow arrow in B).

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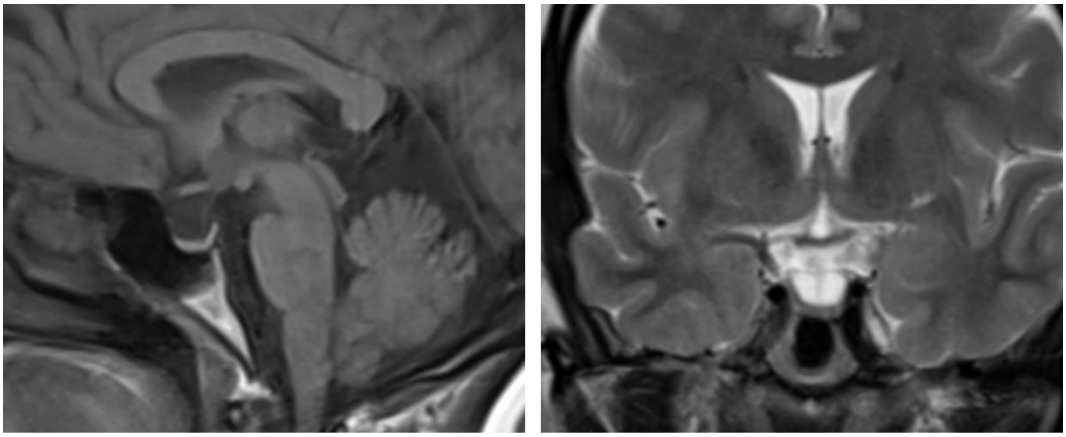

A B

Figure 8: (A) T1 mid sagittal and **(B)** T2 coronal sections of brain in a 64year old male showing concave upper border.

Pituitary height and volume are characteristically directly proportional to its activity. Thus, an increase in the height can be seen in various states of high physiological demand like- puberty, reproductive age group and pregnancy [9-11]. In our study, we observed that pituitary height peaked in the pubertal age group (10-20yrs) and there is gradual reduction in the height and volume with the advancing age. This increase in pituitary height in adolescence is consistent with the increased physiological demand followed by production of various hormones responsible for growth during this period. Similar observation is made in the various other previously done studies as well [12-14]. In few studies, the first peak was observed in 20-30 years age group [15]. A second peak in 50-60 years age group was noted in our study in both male and female sub-groups. Similar findings were noted in study conducted by P. Yadav et al but it was seen exclusively in females. This second peak in pituitary height was attributed to increase in gonadotropin hormone in the study done by P Yadav et al [15]. Thus, volume is a better yardstick to assess pituitary function/ variation with age. Analogous observations were made in a study done on adolescent population by Naik et al [16].

Conclusion:

Most studies suggest that pituitary height is the gauge of pituitary activity and other parameters don't show significant variation with age. In our study pituitary height, length and width showed statistically significant variation with age. But the variation was more avid and substantial in pituitary height and volume. Though we can agree upon the fact that pituitary height is the main variable, the statistically significant variation in length and width cannot be disregarded. This study is aimed at providing the normal morphometric measurements of

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pituitary in Indian population in various age groups and also delineate the normal physiological variations in pituitary size to avoid and pitfalls in evaluation of pituitary gland.

Conflicts of Interest

The authors declared no conflict of interest.

Funding: Nil

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