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IMPACT OF MAGNETIC RESONANCE IMAGING STATUS OF PITUITARY ADENOMAS ON OPHTHALMIC PRESENTATION

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ABSTRACT

Purpose- The aim of this study was to find impact of magnetic resonance imaging (MRI) measured volume of pituitary adenomas (PA) on ophthalmic and clinical presentation.

Methods- A prospective study was done in fifty patients (18 to 67 years), having biochemically or radiologically confirmed pituitary adenomas (PAs). The statistical significance (SS) of association between tumor volume and ophthalmic as well as other clinical features was found.

Results- In 50 subjects, including 31 (62%) males and 19 (38%) females, there was no SS association of age, gender, diminution of vision, headache, squint, field defects, vomiting amenorrhea, loss of libido and acromegaly with tumor volume more than 20.44 mm3 (average tumor volume on MRI). The visual acuity, optic nerve head changes, visual field defects and optical coherence tomography parameters also did not have SS association with MRI volume.

Conclusions- The ophthalmic presentation does not have SS association with the MRI volume of PA.

KEYWORDS : Pituitary Adenoma Size; Magnetic Resonance Imaging; Ophthalmic Features; Optical Coherence Tomography

INTRODUCTION

The magnetic resonance imaging (MRI) is regarded as the modality of choice in the diagnosis of pituitary adenomas (PAs) as it has high resolution. It provides precise anatomical details with respect to extent of tumors and their invasiveness. The contrast enhanced MRI demonstrates the vascularity of tumors and distinguishes these from meningiomas which enhance brilliantly and arachnoid cyst or gliomas which do not enhance or enhance minimally. The coronal scans show the lateral growth of PAs along with its relation to the adjacent parasellar structures such as the internal carotid arteries, which are the most important structures to avoid during surgery. (1)

Several authors have attempted to construct an MR classification based on pneumoencephalography and on radiographic and operative findings, which could tell the tumor size, tumor extent and the relationship to juxtasellar structures, thus giving a clue for prognosis. (2)(3)(4) Edal et al found that larger tumors are more invasive and are found in higher age group and were more often secretory adenomas. (4) On the other hand, Abouaf et al stated that non-functional pituitary adenoma (NFPA), being hormonally inactive, are diagnosed later than secretory tumors and often with larger tumor volume. (5) A larger initial adenoma size was predictor of incomplete remission and uncontrolled disease, thus the authors felt that initial tumor size helps to risk stratify patients regarding expected outcome.(6)

However, very few studies have been done to find relation between MRI size of tumor with demographic, ophthalmic, systemic and hormonal features.

PAs are the third most common primary intracranial tumors in neurosurgical practice. (7) In sella turcica, these lie in close proximity to the optic chaisma. A parasellar growing adenoma can involve the cavernous sinus thus visual dysfunction is one of the most common symptoms of PA which is caused by direct compression to the optic chiasma or disturbance in the optic chiasma's blood supply system.

The large sized PAs can cause symptoms and signs due to mass effect as well as possible hyper-secretion of one or more pituitary hormones, and invasive involvement of the surrounding structures whereas the compression of the pituitary itself can lead to hypopituitarism.(1) PAs can affect ophthalmic status through secretion of hormones like thyroid hormone, through invasion being in close proximity to optic nerve and chiasma, through interruption of blood supply, through cavernous sinus invasion, through its own compression leading to hypopituitarism and through incomplete remission seen in large sized tumors. (8) (9) All these factors have heightened effect when the tumors are larger in size.(7)

An important but relatively less often studied domain of PAs is the impact of MRI size of pituitary tumors on pre-treatment presentation of subjects including demographic, ophthalmic, systemic and hormonal features. Though secretory (functional) and non-secretory (non-functional) nature of PA make a large difference in presentation of two types of subjects, yet their relation with their MRI size have been rarely studied. We conducted a study on subjects of PA while examining the demographic, ophthalmic, systemic and hormonal features and finding the size of their in both secretory and non-secretory adenomas using MRI.

MATERIALS AND METHODS

The present study was done at the Department of Neurosurgery in collaboration with Department of Pathology, Gobind Ballabh Pant Institute of Postgraduate Medical Education and Research (GIPMER) and Department of Ophthalmology, Guru Nanak Eye Centre and Maulana Azad Medical College, New Delhi. The study was approved

by the institutional ethical committee of Maulana Azad Medical College, New Delhi (vide number F. No.16/IEC/MAMC/2016/ Neurosurgery). A written informed consent was obtained from all the participants.

A total of fifty patients in the age range of 18 to 67 years including 30 males (60%) and 20 (40%) females having PAs were enrolled into this prospective study. The subjects who were previously operated cases with recurrence of adenoma; and subjects with other causes of vision deterioration like cataract, corneal opacity, glaucoma; and retinal, optic nerve pathology and central nervous system disease were excluded from the study. History was also taken for visual symptoms like diminution of vision, headache, eye pain, diplopia/squint, field defects, colour vision; and other symptoms like vomiting, amenorrhea, and symptoms of acromegaly like enlarged hands and feet, frontal bossing, etc. All patients were evaluated by ophthalmic, neurosurgical, and endocrinological specialists.

The ocular examination included recording best corrected distance visual acuity following refraction on self-illuminated ETDRS acuity charts at 4 m, under uniform illumination and ETDRS acuity log score which patient could read completely was recorded. The ETDRS charts had 5 letters per row and each letter being assigned value of 0.02 logMAR units. The fundus examination was done for optic nerve head changes in terms of cup to disc ratio using direct ophthalmoscope. The visual field defects were recorded on the Humphrey's Field Analyzer (Humphrey Field Analyzer II, Carl Zeiss Meditec) using the 24-2 testing protocol by SITA-Standard strategy. The subjects also underwent baseline examination with spectral domain optical coherence tomography (SD-OCT) (RTVue; Model iVue 100; Version 2.6; Freemont, CA) for parameters of retinal nerve fibre layer (RNFL) and retinal ganglion cell complex (GCC). The SD-OCT was done by acquiring image on 6x 6 mm area centred over the optic nerve head, by a single technician, in order to study RNFL thickness and optic nerve head parameters, while GCC thickness was measured at macula.(10) The machine was properly aligned after seating the subject with the chin comfortably resting on the chin rest. The OCT lens was adjusted for the patient's refractive error while the contralateral eye was covered. All scans were done using the internal fixation target in the OCT device. Care was taken to ensure no missing areas in the scan due to blinks or eye motion.

The serum hormonal levels of pituitary hormones including growth hormone (GH) in ng/ml, prolactin (PRL) in ng/ml, adeno-corticotrophic hormone (ACTH) in pg/ml, thyroid stimulating hormone (TSH) in milliinternational unit/litre, follicle stimulating hormone (FSH) in milliinternational unit/ml and luteinizing hormone (LH) in milliinternational unit/ml were assessed. The GH levels were determined through suppression test. For a suppression test, 2 ml sample of blood was drawn after 10-12 hours of fasting and then timed blood samples were drawn at 30 minutes, 60 minutes, 90 minutes and 120 minutes i.e. for two hours, after giving them a standard glucose solution (usually 75 grams of glucose) to drink. If the GH level does not drop to below 1 ng/ml during oral glucose tolerance test, the subject has acromegaly. The blood levels of GH at 120 minutes were included in the study.(11) For PRL, the sample was typically collected at 3 to 4 hours after waking. The TSH, ACTH, LH and FSH levels were tested from blood samples. The subjects were divided into secretory/ functional (if any of the serum hormone level was raised) and non-secretory/non-functional category (if none of the serum hormone level was raised). The insulin growth factor (ng/ml) and serum cortisol levels (microgram/dl) were also determined.

The MR imaging of the brain was performed with high resolution T1 and T2 weighted serial sections obtained in the sagittal, axial and coronal planes on a 1.5 Tesla MR scanner to look for cystic changes, necrotic changes or haemorrhages and post contrast SE (spin echo) T1 weighted images were obtained in coronal, sagittal and axial planes to see the vascularity of tumors and enhancement pattern, in order to confirm the diagnosis of PA (which have homogenous or heterogenous enhancement). The MRI volume of tumors was calculated by using formula (antero-posterior diameter x cranio-caudal diameter x transverse diameter)/2 to find single value in mm3.(12) Thus the average MRI volume of PA was found in our subjects.

The patients underwent standard treatment procedure for resection of PAs by transcranial or transnasal-transsphenoidal approach.

The ophthalmic examination to measure the ophthalmic parameters was conducted again at three months after surgery. The post-treatment ophthalmic parameters were compared with the pre-treatment values and SS of mean difference (pre-operative minus post-treatment) was studied in subjects having MRI volume of tumor more than 20.44 mm3 (average MRI volume of PAs in our subjects).

The primary outcome parameter was MRI volume of PA. The secondary outcome parameters were ophthalmic features including visual acuity, visual field defects, and OCT parameters.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) 17 software (SPSS Inc, USA) was used for the statistical analyses. Qualitative data was expressed in percentages/proportions, and quantitative data was expressed in mean and standard deviation; Chi-square test/ Fisher's Exact Test were used for qualitative data and ANNOVA, TUKEYS test, and Student t test was used for quantitative data. The paired t-test was applied in case of normal distribution and Wilcoxan signed rank test was applied for non-normal distribution. SS of association between MRI volume of PA with demographic, systemic, hormonal and ophthalmic features including visual acuity, fundus changes, visual field and optical coherence tomography parameters was found; p value <0.05 was considered statistically significant (SS).

RESULTS

A prospective study in fifty patients (18 to 67 years) including 31 (62%) males and 19 (38%) females having PA was done to study impact of their MRI volume on demographic, systemic, ophthalmic and hormonal features. The mean age of subjects was 4011.9 years; the mean age of males was 40.10 13.10 years, while mean age of females was 36.959.28 years. The mean duration of symptoms at presentation was 19.1±27.3 months (3 months to 12 years). The non-secretory PAs (non-functional PA; NFPA) presented at 10.93 6.92 months (range 3 months-12 years) and secretory PAs (functional PA; FPA) presented at 26.7332.83 months (range 3 months-12 years).

The number of subjects having diminution of vision were 43 (86%), headache 43 (86%), diplopia 04 (8%), visual field defects 14 (28%) and defective colour vision 04 (8%). The number of subjects having vomiting were 01 (2%), menstrual irregularities 06 (12%), loss of libido 02 (4%), and acromegaly 11 (22%). The PA was secretory (FPA) in 28/50 subjects (56%) and non-secretory (NFPA) in 22/50 subjects (44%). The gender distribution showed that out of 28 secretory adenomas, there were 12 (42.9%) males and 16 (57.1%) females, while out of non-secretory adenomas, there were 18 (81.8%) males and 4 (18.2%) females. The mean age of subjects in FPA was 34.2±7.95 years while mean age of subjects having NFPA was 45.8±12.52 years (SS different; p value=0.004; one way Annova test).

The MRI volume of PAs varied from 2.0 mm^3 to 73.66 mm^3. The average volume of PAs on MRI radiological films in our subjects was 20.44 mm^3. The 24 subjects had volume equal to or more than 20.44 mm^3, while 26 subjects had volume less than 20.44 $mm.^3$

Table 1 Shows Mean Size Of Tumors In Two Genders And In FPA & NFPA; Secretory PA Are Larger

S. No.	Pre-treatment stage Volume of tumor varied from 2.0 to 73.66 mm3		P- value for SS of difference
1.	Males	20.38±16.89 mm3	0.48*
2.	Females	20.54±8.93 mm3	
3.	Secretory PA	21.09±14.96 mm3	0.65*
4.	Non-secretory PA	18.61±12.51 mm3	

* Non parametric test - Independent Samples Kruskall Wallis Test

The mean volume of tumor in males was 20.38±16.89 mm^3 and the mean volume in females was 20.54±8.93 mm^3. The mean volume of FPA was 21.09±14.96 mm^3 and mean volume of NFPA was 18.61±12.51 mm^3. The table 1 shows that volume of PAs was larger in females than males (Not SS; p=0.48). Additionally, FPA were larger than NFPA (Not SS; p=0.65).

Table 2 Shows SS Of Association Between MRI Volume Of PAs With Demographic, Ophthalmic And Hormonal Symptoms; None Had SS Association (t Test For Quantitative Variables And Chi Square Test For Qualitative Variable)

S. No.	Parameters	MRI Size<20.44mm3; n=26	MRI Size20.44mm3; n=24	P value
1.	Age range ± SD	39.00±11.82 years	38.67±11.96 years	0.92

2.	Number of males: females	18 (69.23%): 8 (30.77%)	13 (54.2%):11 (45.8%)	0.27
3.	Diminution of vision	21 (80.8%)	22 (91.7%)	0.42*
4.	Headache	23 (88.5%)	21 (87.5%)	1.00*
5.	Squint	1 (3.8%)	3 (12.5%)	0.34*
6.	Field defects	6 (23.1%)	8 (33.3%)	0.42
7.	Vomiting	1 (3.8%)	0 (0.0%)	1.00*
8.	Amenorrhea	2 (7.7%)	4 (16.7%)	0.41*
9.	Loss of libido	1 (3.8%)	1 (4.2%)	1.00*
10.	Acromegaly	6 (23.1%)	5 (20.8%)	0.85

*Fisher's Exact Test

Among the subjects having MRI volume less than 20.44 mm,3 the mean age was found to be (39.00±11.82 years), the number of males were 18 (69.23%) and females were 8 (30.77%). The number of subjects having diminution of vision were 21 (80.8%), headache 23 (88.5%), diplopia/squint 1 (3.8%), and visual field defects 6 (23.1%). The number of subjects having vomiting were 1 (3.8%), amenorrhea were 2 (7.7%), loss of libido 1 (3.8%), and acromegaly 6 (23.1%). Out of subjects having MRI volume equal to or more than 20.44 mm,3 the mean age was found to be 38.67±11.96 years and the number of males were 13 (54.2%) and females were 11 (45.8%). The number of subjects having diminution of vision were 23 (95.8%), headache 21 (87.5%), diplopia 3 (12.5%), and visual field defects 8 (33.3%). The number of subjects having vomiting were 0 (0.0%), amenorrhea 4 (16.7%), loss of libido 1 (4.2%), and acromegaly 6 (25.0%). There was no SS difference between two tumor volumes (MRI Size<20.44mm3 and MRI Size20.44mm3) w.r.t. demographic, ophthalmic or hormonal symptoms.

Table 3 Shows Statistical Significance Of Association Between MRI Volume Of PA With Visual Acuity And Fundus Changes; No SS Association

S. No.	Ophthalmic Parameter	MRI Size 20.44mm3; n=24 (100%)	MRI Size <20.44mm3; n=26 (100%)	P value
1.	Visual acuity right eye ≤ 6/12 (logmar ≥0.3)	18 (75.0%)	17 (65.38%)	0.54
2.	Visual acuity right eye > 6/12 (logmar < 0.3)	6 (25.0%)	9 (34.61%)	
3.	Visual acuity left eye ≤ 6/12 (logmar ≥0.3)	21 (52.5%)	20 (76.92%)	0.29
4.	Visual acuity left eye > 6/12 (logmar < 0.3)	19 (47.5%)	6 (23.07%)	
3.	Optic disc Cup dimensions in right eye ≥ 0.5	9 (37.5%)	15 (57.69%)	0.17
4.	Optic disc Cup dimensions in right eye < 0.5	15 (62.5%)	11 (42.30%)	
5.	Optic disc Cup dimensions in left eye ≥ 0.5	10 (41.7%)	15 (57.69%)	0.39
6.	Optic disc Cup dimensions in left eye < 0.5	14 (58.3%)	11 (42.30%)	
7.	Optic disc pallor in right eye	11 (45.8%)	10 (38.46%)	0.77
8.	Optic disc pallor in left eye	11 (45.8%)	16 (61.53%)	

The SS of association was determined separately for right and left eyes of subjects as PAs affect both right and left eyes, maybe to unequal extents. Table 3 shows that there was no SS association between MRI volume of PA with visual acuity in both right and left eye; Additionally, there was no SS association between MRI volume of PA and fundus changes in terms of optic disc cup dimensions and optic disc pallor in right and left eye.

On calculating SS association between MRI volume of PA and visual field, it was found that none of the parameter had a SS association except visual field PSD value >6 in left eye, which had a SS association with MRI tumor volume > 20.44 mm.3 This means that a larger MRI volume is SS associated with PSD value more than 6. None of the optical coherence tomography parameters including RNFL, GCC, FLV and GLV had a SS association with MRI volume of PA.

Table 4 Shows SS Of Association Between MRI Volume Of PA With Visual Field And OCT Parameters

S. No.	Ophthalmic Parameter	MRI Size20.44mm^3; n=24 (100%)	MRI Size<20.44mm^3; n=26 (100%)	P value
1.	MD value > 6 in right eye	23 (95%)	23 (88.46%)	0.50
2.	MD value > 6 in left eye	22 (91%)	20 (76.92%)	0.10
3.	PSD value > 6 in right eye	22 (91%)	22 (84.61%)	0.98
4.	PSD value > 6 in left eye	21 (87%)	18 (69.23%)	0.06
3.	GCC average in right eye <91.79µm	22 (91%)	22 (84.61%)	0.44
4.	GCC average in left eye <91.79µm	19 (79%)	22 (84.61%)	0.61
5.	FLV in right eye >1.47µm	23 (95%)	25 (96.15%)	0.98
6.	FLV in left eye >1.47µm	22 (91%)	24 (92.30%)	0.50
7.	GLV in right eye >7.9µm	23 (95%)	22 (84.61%)	0.18
8.	GLV in left eye >7.9µm	18 (75.0%)	22 (84.61%)	0.37
9.	RNFL Superior hemisphere in right eye<105.7µm	22 (91%)	23 (88.46%)	0.44
10	RNFL Superior hemisphere in left eye<105.7µm	22 (91%)	21 (80.76%)	0.44
11.	RNFL Inferior hemisphere in right eye<98.6µm	21 (87%)	20 (76.92%)	0.20
12.	RNFL Inferior hemisphere in left eye<98.6µm	22 (91%)	21 (80.76%)	0.33

MD= Mean Deviation; PSD= Pattern Standard Deviation; GCC= Ganglion cell complex; FLV= Focal loss of volume; GLV= Gross loss of volume; RNFL= Retinal Nerve Fibre layer

Out of a total of 28 secretory adenomas, 17 subjects had prolactinomas (9 had MRI size more than 20.44 mm3), 08 had somatotrophic adenoma (Growth hormone secretors) (5 had MRI size more than 20.44 mm3), 03 had combined prolactinoma and somatotrophic adenoma (both prolactin and growth hormone secretion) (2 had MRI size more than 20.44 mm3), 02 had adenocortico-trophic hormone secretion (0 had MRI size more than 20.44 mm3), 02 had thyroid stimulating hormone secretion (0 had MRI size more than 20.44 mm3), none had follicle stimulating hormone secretion, and none had luteinizing hormone secretion. The subjects having raised insulin growth factor was 9 (4 had MRI size more than 20.44 mm3) and subjects had reduced serum cortisol 20 (13 had MRI size more than 20.44 mm3).

Table 5 Shows Associations Between MRI Tumor Size With Serum Hormonal Levels

S. No.	Parameters	MRI Size < 20.44 mm^3 n=24	MRI Size 20.44 mm^3 n=24	P value
1.	Raised Serum Prolactin	8	9	0.62
2.	Raised Serum Growth Hormone	3	5	0.46*
3.	Raised Serum Prolactin and Growth Hormone	1	2	0.60*
3.	Raised Serum Insulin growth factor	5	4	1.00*

4.	Raised Serum luteinizing hormone	0	0	-
5.	Raised Serum follicle stimulating hormone	0	0	-
6.	Raised Serum adeno-corticotrophic hormone	2	0	0.49*
7.	Raised Serum thyroid stimulating hormone	2	0	0.49*
8.	Reduced Serum cortisol	7	13	0.049

*Fisher's Exact Test

There was no SS difference between two tumor volumes (MRI Size<20.44mm3 and MRI Size20.44mm3) w.r.t. deranged serum hormonal levels except for reduced serum cortisol (p=0.049)

Table 6 showing the preoperative mean values and postoperative mean values and their mean difference (pre-operative minus post-operative) along with statistical significance of mean difference in subjects having MRI volume of tumor 20.44mm3; Test applied - Paired T test for normal distribution and Wilcoxan Signed Rank Test for non-normal distribution

S. No.	Variable	Preoperative mean SD	Postoperative mean SD	Mean Diff	% change	P value
1	Visual Acuity (logmar)	0.78 ± 0.56	0.71 ± 0.62	0.07	8.97	0.01
2	Cup dimensions	0.44 ± 0.16	0.48±0.19	-0.04	9.09	0.01
3.	Visual Fields Analysis					
	MD	-18.3 ± 7.8	-14.8 ± 6.9	-3.44	18.77	0.03
	PSD	13.19 ± 5.0	13.5±4.4	-0.31	02.35	0.01
4	OCT GCC (µm)					
	Average	80.3 ± 16.7	74.5 ± 12.5	5.75	7.15	0.01
	Superior	81.21±17.2	74.2±13.1	6.92	8.52	0.01
	Inferior	79.29±16.99	74.71±13.60	4.58	5.77	0.01
	FLV	7.5 ± 3.5	10.1 ± 6.9	-2.69	35.86	0.06
	GLV	17.4±7.9	21.04±10.15	-3.59	20.57	0.02
5	OCT ONH					
	RNFL Average	80.3±16.9	74.5±12.16	5.78	7.15	0.01
	Superior	83.4±20.2	79.7±18.1	3.67	4.39	0.03
	Inferior	81.8±20.6	77.5±11.5	3.57	4.40	0.01
6	OCT RNFL (peripapillary)					
	SN	95.2±17.6	90.5±12.6	8.1	9.59	0.01
	NU	58.2±22.7	52.8±13.8	7.1	11.75	0.01
	NL	53.8±25.8	43.6±13.3	5.2	9.48	0.01
	IN	103.1±32.7	90.0±23.0	7.3	7.05	0.01
	IT	106.2±31.8	105.6±21.8	4.5	4.04	0.01
	TL	51.3±12.9	59.6±26.5	-3.2	5.72	0.01
	TU	56.4±15.2	53.1±16.1	1.6	2.69	0.01
	ST	114.6±26.7	102.7±26.4	6.5	5.72	0.01
	RNFL average	80.3±16.7	78.5±14.18	1.8	2.24	0.01
	RNFL superior	83.4±20.2	79.7±18.1	3.67	4.39	0.03
	RNFL inferior	81.8±20.6	77.5±11.5	3.57	4.40	0.01

The table 6 shows the preoperative mean values and postoperative mean values and their mean difference (pre-operative minus post-operative) along with SS of mean difference in subjects having MRI volume of tumor 20.44mm.3 The table shows that visual acuity improved after surgery. The optic disc cup:disc ratio did not improve; rather it increased from 0.44 ± 0.16 to 0.48±0.19. While all the OCT and RNFL thickness parameters reduced after resection, RNFL temporal lower quadrant improved (increased from 51.3±12.9 to 59.6±26.5) after resection. It is visible that resection of pituitary adenoma induced a SS difference (shown by p-values) in pre-operative status vis-a-vis post-operative status of ophthalmic features in patients having MRI volume of tumor 20.44 mm3. However, only visual acuity, visual field mean deviation and retinal nerve fibre layer temporal lower quadrant improved after resection, while other ophthalmic parameters deteriorated in patients with MRI tumor volume > 20.44 mm3.

DISCUSSION

Though PA are benign, yet these can cause ophthalmic and neurological symptoms on account of mass effect and secretion of pituitary hormones.(13) The PA are primarily classified according to their size into microadenomas < 1 cm and macroadenomas > or = 1 cm.(7) While incidence of NFPAs is 28-33.2% among PA population, Ferrante et al reported that 96.5% of these tumors present as macroadenomas. (5)(14) Though FPA can exert remote effects through hormonal secretion, but despite having visual defects in 67.8% cases, NFPA due to hormonal inactivity (hypopituitarism), patients are slow to become aware of their visual dysfunction. (5)(14)(15) Abouaf et al also found that NFPAs may lead to blindness and cause visual impairment in 58% cases and more rarely these also cause ocular motor disorder.(5)

While the effects of FPA can be monitored through serum hormonal levels, however for both types of PAs, MRI is being utilised to determine tumor diameter and cavernous sinus invasion to predict long term events and outcome of treatment.(12)

Ludin and Pedersen have stated that use of the largest diameter provides only a rough measure of the tumor size. The authors recommend use of formula 0.5 x width x length x height for providing a fairly adequate estimate of tumor volume.(12) Unlike other authors who studied only diameter of PAs, like Thomas et al we studied MRI volume of PA calculated by antero-posterior diameter x cranio-caudal diameter x transverse diameter/2 to find single value in mm3 and we found if there was any SS association of volume of PA with neuro-ophthalmic and hormonal features. (13)(16)(17)(18) In our study, the volume of secretory PAs was 21.09 14.96 mm3 was more than the volume of non-secretory PAs was 18.6112.51 mm3. Edal et al had similar results while Abouaf et al found that NFPA are larger in size. (4)(5)Abouaf et al stated that non-functional pituitary adenoma (NFPA), being hormonally inactive, present later.(5) But in our study, the non-secretory PAs presented earlier (10.93 6.92 months; range 3 months-12 years) than secretory PAs (26.7332.83 months; range 3 months-12 years). We feel that this must be due to manner of mass effect and manner of invasion of non-secretory PA in our subjects that they turned symptomatic earlier. We did not find any SS association with MRI volume of PA with derangement in serum levels of different hormones except for reduced serum cortisol level (p=0.049) which were SS associated with larger MRI Volume (>20.44 mm3). This means that type of hormonal derangement did not have any relation with volume of FPAs and NFPAs.

In 78 subjects of PA, Ren-Wen et al found 32 (41%) patients experienced blurred vision or visual field defect as an initial symptom. They did brain MRI before surgery to determine pituitary macroadenoma size and investigate quantitative relationship between tumor size and degree of visual impairment, and repeated MRI to assess visual improvement after surgery. The visual impairment score (VIS) was derived by combining the scores of best-corrected visual acuity and visual field. Statistical analysis showed that 1) poor preoperative vision is related to tumor size, displacement of the optic chiasm in the sagittal view on MRI and optic atrophy, and 2) poorer visual prognosis is associated with greater preoperative VIS. In multivariate analysis the only factor significantly related to VIS improvement was increasing PA size, which predicted decreased improvement. Receiver operating characteristic curve analysis showed that PAs larger than 2 cm cause defects in vision while

adenomas 2 cm or smaller do not cause significant visual impairment. The authors concluded that patients with a large macroadenoma or giant adenoma should undergo surgical resection as soon as possible to prevent permanent visual loss.(13)

Musluman et al analysed FPA and NFPA > 3 cm in 49 women and 54 men with mean age of 43.2 years (range 19-66 years) and studied preoperative and postoperative visual acuity, visual field, and ocular fundi and their relationship with the pattern and duration of the symptoms and the size of the tumor. Normalization of visual acuity was obtained in 71.5% of patients, symptoms persisted in 13.6%, and symptoms worsened in 1%. Postoperative improvement of visual field defects (VFDs) was observed in 74.1% of patients. This study shows that patients with severe visual impairment may have remarkable improvement if surgical decompression is done early.(17)

Like Musluman et al, we conducted our study on ophthalmic presentation of both FPA and NFPA. In our study, 26 subjects had an MRI volume less than 20.44 mm3 while 24 subjects had an MRI volume equal to or more than 20.44 mm.3 (17)We found that there was no SS difference of association of complaint of diminution of vision with tumor volume (p=0.42). Our objective assessment also showed that none of the ophthalmic parameter had SS association with tumor volume. Though Ren-Wen et al found poor prognosis in PAs larger than 2 cm, Musluman et al even in FPA and NFPA > 3 cm, found visual impairment score improved postoperatively in 92% of patients.(13) (17) Following surgical resection of PA, we calculated the SS of difference between pre-operative and post-operative ocular parameters in subjects having volume of PA equal to or more than 20.44 mm.3 In our study, we found that only visual acuity, visual field mean deviation and retinal nerve fibre layer temporal lower quadrant improved after resection, while other ophthalmic parameters deteriorated in patients with MRI tumor volume > 20.44 mm3.

In their study on 93 patients of non-secretory PA, Thomas et al found that 88/93 (94.6%) patients had a field defect on automated perimetry using the Humphrey Field Analyzer 30-2 programme. The chi-square test for trend was used to test association of tumour volume seen on CT or MRI scan, with severity of typical defects. All 31 patients (33.3%) with a tumour size greater than 20 cc had field defects. Severity of field defect increased with tumour volume (Chi-square test for trends significant p = 0.0096).(18) On calculating SS association between MRI volume of PA and visual field, we found that in our subjects neither visual field nor OCT parameters had a SS association except visual field PSD value >6 in left eye, which had a SS association with MRI tumor volume > 20.44 mm.3 This means that a larger MRI volume is SS associated with PSD value more than 6 (worse fields).. Similar results were reported by Kim et al, who found that tumor volume was positively correlated with visual field pattern standard deviation (PSD, p = 0.020).(19)

Several authors have studied ocular affections of PAs in form of visual loss, visual field defects, diplopia, optic nerve head changes, proptosis and relative afferent pupillary defect.(20)(21) However, there are very few studies utilizing OCT for finding the ocular manifestations of pituitary adenomas. Newman et al studied six clinical articles describing preoperative ophthalmologic evaluation of adult patients with NFPA and found that GCC thickness is reduced but RNFL thickness is not much affected in patients of pituitary adenoma.(22)

Duru et al found that patients with microadenoma, the mean RNLF thickness of the inferior quadrant decreased significantly in patients with macroadenoma (p=0.046 and p=0.032) as compared to healthy subjects. They concluded that the RNLF becomes thinner in the inferior quadrant in macroadenoma as a result of the chiasmal compression.(23) We also found thinner RNFL in our subjects but there was no SS association between MRI volume of PA with OCT parameters that is RNFL and GCC are not necessarily thinner in larger tumors than RNFL and GCC parameters in smaller tumors. Additionally the OCT parameters did not improve SS following surgery in our subjects having MRI volume more than 20.44 mm3. We feel that the ophthalmic status did not improve in our subjects on account of delayed presentation (3 months-12 years).

Glebauskiene et al evaluated RNFL thickness in PA by OCT and compared it with MRI characteristics of pituitary extension in 154 eyes of 77 PA patients. Ophthalmologic evaluation was performed before surgical treatment. Average and per quadrant thickness of peripapillary RNFL (internal limiting membrane to nerve fiber layer/ganglion cell layer) were calculated in OCT performed in a disc circle mode (layer distance 3.45mm; 1024 scans). Preoperative RNFL thickness around the optic nerve disc was reduced significantly in all four quadrants in PA patients compared with control group (p<0.001) while RNFL thickness was reduced significantly only in the temporal quadrant in PA patients with suprasellar extension compared with the patients without suprasellar extension (p=0.009). Their results indicated that suprasellar extension in PA patients causes visual disturbances.(24) We also feel that though volume of tumors exclusively did not influence various neuro-ophthalmic features in our subjects (none of the symptom had a SS association with tumor volume > 20.44 mm3) as perhaps it was the manner in which PA exerted compressive effect on optic chiasma which mattered more.

We found that that resection of PAs induced a SS difference (shown by p-values) in pre-operative status vis-a-vis post-operative status of ophthalmic features in patients having MRI volume of tumor 20.44 mm3. However, only visual acuity, visual field mean deviation and retinal nerve fibre layer temporal lower quadrant improved after resection, while other ophthalmic parameters deteriorated in patients with MRI tumor volume > 20.44 mm3. This was perhaps because the larger tumor size had already caused a great damage due to their size before the PA could be taken for resection.

Previous authors have generally studied only one type of PAs either FPA or NFPA, but like Musluman et al and Duru et al we have studied outcome in both types of PAs vis-a-vis their MRI size. (13)(17)(18) (22)(23) We studied effect of midline located PA on both the eyes while SS association of MRI size of PAs with laterality of eyes has never been studied before. We found that PSD >6 in left eye of subjects was SS associated with tumor volume > 20.44 mm3. NFPAs are the most frequent pituitary tumors, additionally, visual symptoms from NFPAs are common, thus MRI gains edge as it can find long term outcome in both FPA and NFPA through determination of both size and invasiveness. (21)

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