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Visual Field, Retinal Nerve Fibre Layer Thickness in Pituitary Adenoma – Retrospective Study

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Abstract: Aims and Objectives *– To study visual field presentation in patients with radiologically suspected, histologically proven pituitary macroadenoma and correlation with retinal nerve fibre layer (RNFL) thickness using spectral domain optical coherence tomography in a retrospective study*

Methodology *– Medical records of 23 patients diagnosed with pituitary adenoma confirmed by histopathology report from November 2013 to May 2018 were reviewed. Data of complete ocular examination and MRI-Brain before surgery were noted.*

RESULTS*– 46 eyes of 23 patients(11 male and 12 female) with mean age of 50.95 years, histologically proven pituitary macroadenoma were included. Of 46 eyes, 18 eyes had no visual field defects, 18 eyes had bitemporal hemianopia, 7 eyes had early field defects, 3 eyes with loss of temporal field sparing fellow eye, 8 eyes did not show any RNFL thinning. Of 16 eyes with no field defect, 8 eyes showed retinal nerve fibre layer thinning on sd-oct*

CONCLUSION*– RNFL assessment and visual fields help in better prognostication and understanding of pituitary macroadenoma.*

Keywords – *macroadenoma, sd-oct, RNFL*

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I. Introduction

Pituitary adenomas represent 10-15% of all primary brain tumors[1]. Although benign, some tumors can be aggressive[2] .The tumor is classified based on size as microadenoma, smaller than 10mm, or as macroadenoma when it exceeds 10mm in diameter[3] .Clinically, they present as functioning or non-functioning pituitary adenomas [4] .Visual field defects are thought to be due to the direct compression or the effect on the blood supply of the optic chiasm[5] .A spectrum of visual manifestations has been reported with these tumors, ranging from the absence of any visual symptoms to severe visual field defects and loss of vision. The prevalence of visual field defects in pituitary adenomas varies from 37 to 96% in different studies. The most common visual field defect is bitemporal hemianopia[6,7] .

Visual field defects can be detected by manual perimetry and by automated static perimetry[5].In patients with long standing compression of the optic chiasm, ganglion cells may undergo axonal degeneration[8] .Such axonal loss can sometimes be observed in the optic disc and retina. Optical coherence tomography(OCT) is able to identify retinal nerve fibre layer(RNFL) and ganglion cell loss in retina[9,10] .Magnetic resonance imaging(MRI) demonstrates compression to optic chiasm by the tumor .

Despite on-going advances in the medical and radiotherapeutic management of pituitary tumors, surgical resection remains the therapy of choice for vast majority of these lesions[4] , particularly macroadenomas.

This study was done to assess which changes occurred earlier – visual field defect or retinal nerve fibre layer thinning. The aim of this study also includes to study ophthalmologic findings in patients presenting with radiologically and histologically proven pituitary adenoma.

MRI Image showing Pituitary adenoma

II. Materials and Methods

This retrospective time-bound hospital based study was done in Father Muller medical college hospital, Kankanady, Mangalore, Karnataka from December 2013 to June 2018. A total of 23 adult subjects (both males and females) of aged >=18 years.

Study Design : Retrospective time bound hospital based study

Study Location : This was a tertiary care teaching hospital based study done in Department of Ophthalmology at Father Muller medical college hospital, Kankanady, Mangalore, Karnataka

Study Duration: December 2013 to June 2018

Sample size : 23 patients

Subject and selection method: Cases evaluated in Father Muller medical college hospital for radiologically diagnosed pituitary adenoma with/without visual disturbances who either visited Ophthalmology OPD or were sent to Ophthalmology OPD from Endocrinology OPD were taken from medical records dated from December 2013 to June 2018.

Routine ophthalmologic evaluation which included visual acuity, visual field testing by perimetry, dilated fundoscopy with Fundus photography and Sd-oct(Optical coherence tomography) of retinal nerve fibre layer(RNFL) were done for all these patients.

Waiver of consents taken

Inclusion criteria

1. Patients diagnosed with pituitary adenoma by MRI and histopathology reports who underwent ophthalmologic evaluation.
2. Age between 20 to 75 years
3. Patients in whom OCT RNFL was done at presentation of pituitary adenoma.
4. Patients in whom perimetry was done at presentation of pituitary adenoma.

Exclusion Criteria

1. Presence of pre-existing optic nerve disorders.
2. Presence of pre-existing retinal disorders, vitreous haemorrhages.
3. Presence of past ocular trauma.
4. Patients who were not co-operative for ophthalmologic assessment-perimetry and OCT-RNFL.

III. Ophthalmic Parameters

1 . Visual field by perimetry by HFA 30-2

2. Fundus examination using biomicroscopy with a + 90D lens/indirect ophthalmoscope with +20D lenses / direct ophthalmoscope through dilated pupils (using tropicamide 1% with phenylephrine 2.5% eye drops).Fundus photography were taken and recorded.

3.SD-OCT RNFL was done.

OTHER PARAMETERS

1. MRI REPORT
2. HISTOPATHOLOGY REPORT confirming the diagnosis

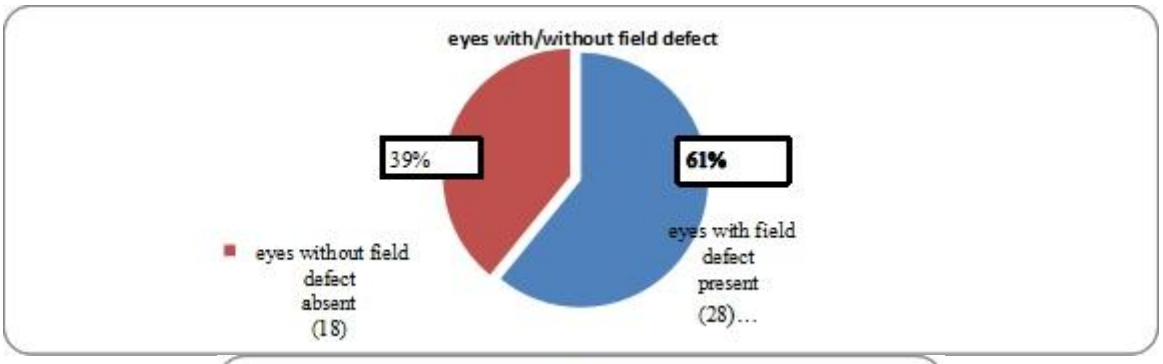
Statistical Analysis : Was done using SPSS software. Collected data was analysed by mean, standard deviation, Frequency and Fishers exact test

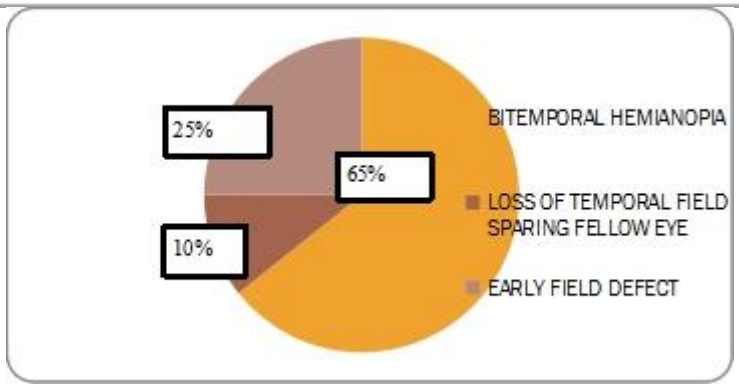
IV. Results

46 eyes of 23 patients(11 males and 12 females) with mean age of 50.95 years with histologically proven pituitary adenoma were included.

Table 1- Visual field pattern is as follows:

	VISUAL FIELD PATTERN	NUMBER OF EYES(SUBJECTS)	PercentageEyes(subjects)
I	BITEMPORAL HEMIANOPIA	18(9)	39.13%(39.13%)
II	LOSS OF TEMPORAL FIELD SPARING FELLOW EYE	3(3)	6.52%(13.04%)
III	EARLY FIELD DEFECT	7(4)	15.21%(17.39%)
IV	NO FIELD DEFECT	18(10)	39.13%(43.47%)





This table 2 shows the age-wise distribution with number of eyes affected (number of subjects)

Age group(years)	I	II	III	IV
20-40	4(2)	1(1)	2(1)	3(2)
41-59	14(7)	1(1)	2(1)	7(4)
60-75	0	1(1)	3(2)	8(4)
TOTAL SUBJECTS	18(9)	3(3)	7(4)	18(10)

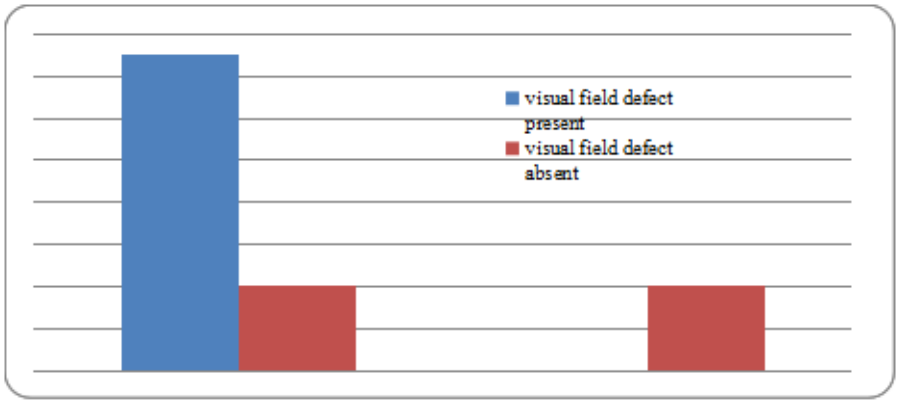
The table 3 shows correlation direct correlation between visual field defect and decreasing visual acuity.(P value = 0.008 by Fishers exact test, highly significant)

Visual acuity	Visual field defect +	No visual field defect
Counting finger -1 m to 6/36	16 eyes	-
6/24 to 6/12	14 eyes	7 eyes
Better than 6/12	-	9 eyes

This table 4 shows number of subjects with/without RNFL changes with respect to visual field

Visual field defect/OCT RNFL changes	present	absent
present	15	-
absent	4	4

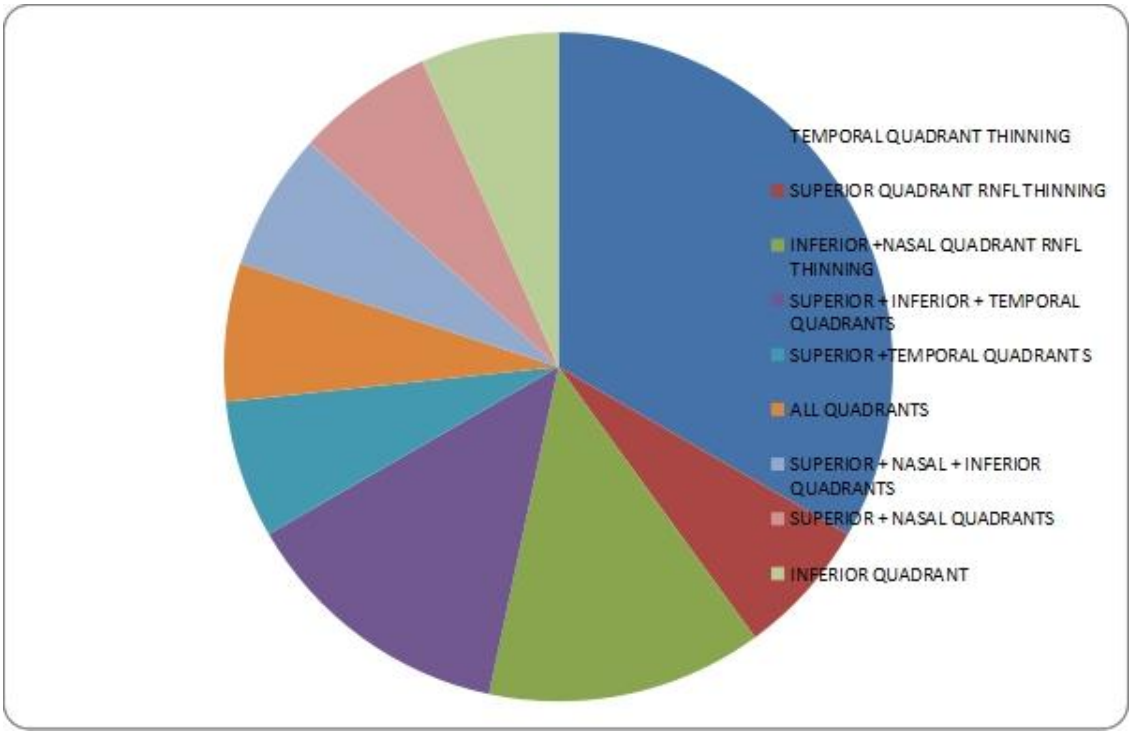
OCT-RNFL changes were noted irrespective of presence or absence of visual field defect.
Retinal nerve fibre layer thinning – early indicator before the onset of visual field defect
(p value = 0.001 by chi-square test , highly significant).



X axis – OCT RNFL changes .
Y axis – number of eyes

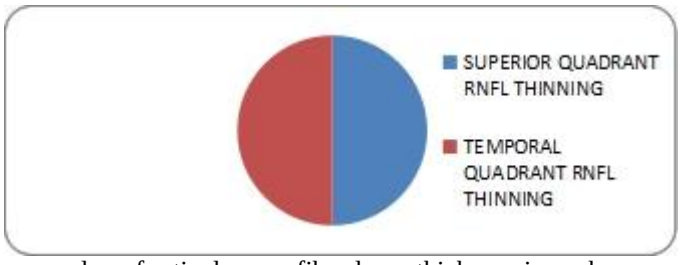
The following table 5 shows number of eyes along RNFL thinning in corresponding quadrant/quadrants in subjects with visual field changes

OCT-RNFL FINDINGS	NUMBER OF EYES(SUBJECTS)
TEMPORAL QUADRANT RNFL THINNING	7(5)
SUPERIOR QUADRANT RNFL THINNING	2(1)
INFERIOR QUADRANT RNFL THINNING	1(1)
INFERIOR +NASAL QUADRANT RNFL THINNING	4(2)
SUPERIOR + INFERIOR + TEMPORAL QUADRANTS	4(2)
SUPERIOR +TEMPORAL QUADRANTS	1(1)
ALL QUADRANTS	2(1)
SUPERIOR + NASAL QUADRANTS	1(1)
SUPERIOR + NASAL + INFERIOR QUADRANTS	2(1)



This table 6 shows number of eyes along RNFL thinning in corresponding quadrant/quadrants in subjects with visual field changes

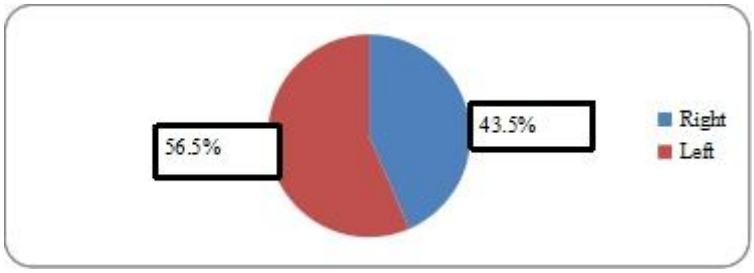
OCT-RNFL FINDINGS	NUMBER OF EYES(SUBJECTS)
TEMPORAL QUADRANT RNFL THINNING	4(2)
SUPERIOR QUADRANT RNFL THINNING	3(2)



This table 7 shows the mean value of retinal nerve fibre layer thickness in each eye quadrantwise in this study along with their standard deviation and comparison with normative data

Quadrants	Right eye	Left eye	Normal values
Superior	82.91 +/- 37.661	89.69 +/- 34.626	113.11 +/- 8.80
Nasal	56.91 +/- 15.658	56.73 +/- 15.639	72.32 +/- 7.09
Inferior	94.65 +/- 39.318	94.17 +/- 36.431	120.82 +/- 9.16
Temporal	45.13 +/- 10.323	43.60 +/- 9.557	61.43 +/- 6.30

Based on laterality, left eyes were more affected than right eyes.



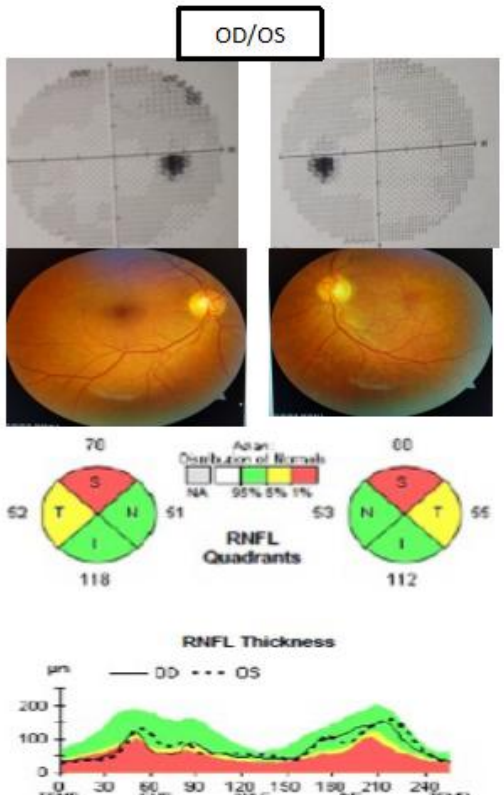
V. Discussion

Pituitary adenomas are generally slow-growing, benign neoplasms which can compress the optic chiasm or optic nerve causing visual loss or visual field defects. Anatomic relationships suggest that tumor extension 10 mm above the diaphragmasellae is necessary for the anterior visual pathway to become compressed. Because lesions that damage the body of the optic chiasm characteristically produce bitemporal hemianopia [15], bitemporal field changes were the most common field defects on presentation in pituitary adenoma

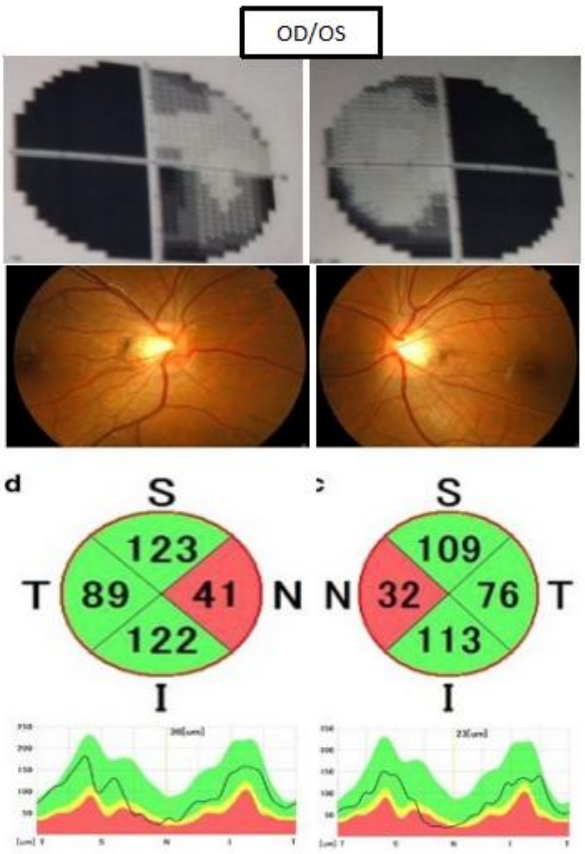
When the optic chiasm is directly compressed, or its blood supply is affected by a pituitary adenoma, retinal ganglion cell (RGC) axonal injury and visual dysfunction will occur. The three main postulated pathological mechanisms are disruption of conduction along the axon, impairment of axoplasmic flow and demyelination with impaired signal conduction[16].

The physiological relationship between the retina and optic chiasm ensures that damage to the optic chiasm will affect the retina, especially the RNFL, which comprises RGC axons. RNFL thinning indicates the loss of ganglion cell axons due to long-term chiasmal lesions.

Visual Field defects are the most common and usually the earliest symptom of visual disturbance due to direct compression of the crossing fibers in the optic chiasm by pituitary adenomas. As the disease develops, the macular fibers can be affected and cause other visual dysfunctions, such as Visual Acuity damage, color vision loss and optic disc pallor. However, Visual Acuity impairment, color vision loss, and optic disc pallor are strongly associated with the degree of VF defect[17,18]



OCT-RNFL changes in individuals with normal visual fields- retinal nerve fibre layer thinning noted.



OCT-RNFL changes noted in cases with bitemporal hemianopia- retinal nerve fibre layer thinning noted.

In this study, as the patients presented late for eye evaluation, there is not only visual field loss, but there is also loss of visual acuity as seen in our study (p value=0.001). 5/23 patients in our study presented with total vision loss, 13/23 patients in this study presented with partial vision loss. Rest 5 patients had no visual complaints, but had endocrinologic abnormalities such as prolactinoma, who were diagnosed with pituitary adenoma and was referred to ophthalmology OPD for eye evaluation. As classically described in previous studies, our study also showed that most common visual field loss is bitemporal hemianopia(65%). In our study 15 out of 23 subjects had visual field defects detected by Humpreys Field Analyser(HFA) also had significant retinal nerve fibre layer thickness(p value=0.008). Interestingly 8 subjects diagnosed with pituitary adenoma who were sent for routine ophthalmological evaluation of visual field and RNFL assessment had no visual field defects. Out of 8 subjects whom visual field defect was not seen, 4 of them had retinal nerve fibre layer thinning.2/4 had RNFL thinning in superior quadrant, 2/4 had RNFL thinning in temporal quadrant

The degree of RNFL thinning due to compression of sellar tumors has been found to be correlated with visual field defects [20]. OCT is a useful tool for objective and quantitative assessment of the structural and functional damage of RNFL and GCC in eyes with optic nerve impairments caused by chiasmal compression[21]. RNFL and GCC thickness measured by OCT has been identified as useful prognostic indicators in the preoperative assessment of chiasmal compression. SD-OCT may have a role in the early diagnosis and management of patients with pituitary tumours by detecting retinal nerve fibre layer thinning preceding visual field defects.

In this study, 11/23 patients in this study had normal disc findings in both eyes of which 11 eyes in 8 patients have RNFL loss.12 eyes of 8 patients had disc pallor which was significantly corresponding to RNFL loss seen in sd-oct. 4 patients in the study had neuroretinal rim thinning which corresponded to RNFL loss seen in sd-oct. In this study, retinal nerve fibre layer values in each quadrant in either right or left side was assessed and average retinal nerve fibre layer thickness was higher in right side in all quadrants except superior quadrant . Left eye was most affected in this study(56.5%). Minimum RNFL thickness left behind was 32 in superior quadrant in those who had retinal nerve fibre layer thinning without visual field defects.Minimum size of pituitary adenoma on MRI scan that caused RNFL changes was 9.5 mm in those without field defects and 10 mm in those who had field defects. Minimum RNFL thickness left behind in those with visual field defects was 18 in bitemporal hemianopia and 31 in other field defects. This provides evidence that patients with field loss have significant RNFL thinning than those without field loss. Also, patients with bitemporal field loss have denser RNFL loss than other field defects.

Surgical removal is a common therapy for pituitary adenoma and can generally improve the visual function of patients with visual symptoms complaints[19].

There is a need for increasing awareness among the ophthalmic community and other physicians for timely referral of these patients and prompt neurosurgical intervention.

VI. Conclusion

Visual field analysis and Optical coherence tomography- retinal nerve fibre layer (RNFL) thickness aids in the prognostication and better understanding of pituitary adenoma.

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