Clinico-radiological factors affecting visual recovery in pituitary tumours

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ABSTRACT

Objectives: It is a prospective, single institute, observational study; primary outcome measure; factors determining visual field improvement and secondary outcome measure; the relationship between severity of visual impairment and duration of symptoms.

Material and Methods: It is a prospective, single institute, observational study that will be conducted between January 2020 and January 2022 in the department of Neurosurgery at the G. R. Medical College & JAH Group of Hospitals, Gwalior (M.P.), a tertiary centre in India. All patients were admitted to the neuro-surgery department & operated on basis of a CT scan of head/MRI findings. Patients with Laboratory findings having hypopituitarism, diabetes insipidus (DI), and hyperprolactinemia and willing to undergo Endocrinological & visual field tests in inclusion criteria. Data obtained from the study will be analyse by using appropriate statistical tests or methods.

Results: At present, series most common age presentation (36.7%) between 21-30 years. In our study, of the total patients, 60% were males and 40% were females. The male to female ratio is 2:1 most common complaint of vision loss and only 50% had hormonal symptoms. In our study 46.7% patients have duration of symptoms < 6 months and 6/6 - 6/24 visual acuity was present in 73.3% patients & 13.3% had optic atrophy (primary/secondary), 43.3% patients had bi-temporal hemianopia. In our study Suprasellar extension was present in 90% of patients & Vascular invasion was seen in 26.7% of patients.

Conclusion: Good results are seen in patients who have a lesser duration of symptoms, and good pre-operative visual acuity has improved the final visual outcome. Post-operative visual recovery is most promising after 3 months to 1 year of surgery. Immediate results of visual recovery should not be expected. Most patients presented with larger adenomas had poor visual recovery as compared to small adenomas. Patients who underwent endoscopic trans-nasal, trans-sphenoidal resection had better post-operative recovery.

INTRODUCTION

Pituitary adenomas account for 10-15% of all brain tumours, it is the third most frequently diagnosed brain tumour [1]. Pituitary tumours can be clinically Classified as functioning & non-functioning pituitary adenomas [2]. Non-functioning pituitary adenomas are not usually associated with

Keywords

pituitary adenoma, tumours, visual field defect, hormonal symptoms

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Clinical syndromes related to hormone excess and may be discovered occasionally.[3]

When they exert mass effects on surrounding tissues leading to visual impairments, headache and hypopituitarism and hydrocephalus.[4]

The growing of pituitary tumors may compress the surrounding structures especially optic nerve, cause visual field defects including bitemporal hemianopia, visual disturbance. The frequency of visual field defects in pituitary adenomas varies from 37% to 96% in different studies.[5]

The symptoms due to pituitary hormonal dysfunction are not the one for which the patient seeks medical attention.

The presence of a visual field defect is one of the common indications for surgery in patients with pituitary tumors, and the degree of the visual field defect should be identified through a preoperative visual field examination, even if the patient does not complain of symptoms [6]

If the tumor is accompanied by a visual field defect, it is clinically important to predict the prognosis for postoperative visual field recovery.[7]

The typical visual field defect, bitemporal hemianopia, is due to anatomical compression of the optic chiasm, which contains the crossing nasal fibres of each optic nerve fibres.[8]

**MATERIALS AND METHOD**

**Study Design**

It is a prospective, single institute, observational study will be conducted between January 2020 and January 2022 in the department of Neurosurgery at the G. R. Medical College & J.A. Group of Hospitals, Gwalior (M.P.), a tertiary centre in India. The study protocol will be approved by the Institutional Ethics Committee and written informed consent will be obtained from all participants.

**Sample Size**

30 and above Patients

**Inclusion criteria**

1. All patients admitted in neuro-surgery department & operated on basis of CT scan of head/MRI findings.
2. Patients with Laboratory findings having hypopituitarism, diabetes insipidus (DI), and hyperprolactinemia.
3. Patients willing to undergo Endocrinological & visual field tests.
4. Patients with visual field defect induced by pituitary tumors.

**Exclusion criteria**

1. Severe co-morbid illness
2. Patients having past h/o of surgery or treatment adjacent to Sellar lesion.
4. Patients not willing for operation.
5. Patients less than 15 years of age.
6. Cases with other causes of visual loss such as cataract, Glaucoma, and Retinal detachment.

**Study Protocol and Data Collection**

All patients of pituitary tumour admitted in department of Neurosurgery. A written consent will be taken from the patient or their attendants for the study. Details of demographics and detailed history of event, presenting symptoms and signs, laboratory parameters (Serum prolactin, Growth hormone, ACTH, TSH, Cortisol) and imaging findings (size of tumour, invasion of surrounding structures) A contrast-enhanced magnetic resonance imaging (MRI) of the sella was performed in all these patients preoperatively. The adenoma volume was calculated by the De Chiro and Nelson formula [volume = (sagittal × coronal × axial diameters) × π/6]. Modified Hardy's classification was used for staging (extension) and grading (degree of sellar destruction) of the pituitary adenomas. We also used Knosp grading to document the parasellar extension, Ophthalmologic evaluation (Visual acuity, Visual field, Fundus) VA was determined by the Snellen's chart, and VF testing was performed by Humphrey automated computerized perimeter, C76 Panel (Carl Zeiss, Germany). In patients with finger counting, hand movement, and only perception of light, the assessment of VF was done manually using confrontation test before surgery & After 1 month & 3 months of surgery will be noted. The results were recorded as follows: (i) No change, (ii) improved, and (iii) worsened. Significant improvement/worsening was defined as any grade improvement or deterioration in the VA and VF, based upon a 30% change to avoid inter- and intra-individual variation, according to John Thomas Smith's rule of the one-third. Blindness was defined as absence of
perception of light. Management of the patients will be planned and observe in terms of outcome.

**Outcome Measure**
1. Primary outcome measure- Factors determining visual field improvement.
2. Secondary outcome measure- relationship between severity of visual impairment & duration of symptoms.

**Data Analysis**
Data obtained from the study, will be analyse by using appropriate statistical test or methods. Data will be entered in Microsoft Word and analyzed using SPSS version 16.0 and EPI INFO version 7.0. Appropriate statistical test will be applied to analyze the data.

**RESULTS**
In present series (N=4) 13.3% patients were up to 20 yrs. of age, (N=11)36.7% between 21-30 years, (N=8)26.7% between 31-40 yrs., (N=5)16.7% were between 41-50 yrs. & (N=2) 6.7% between 51-60 yrs. Our study of the total patient 30, (N=18) 60% were males & (N=12) 40% were females. The male to female ratio is 2:1.

In the present study (N=24) 80% of patient had complaint of Headache, Vision loss was present in (N=25) 83.3% of patients & Features of Raised ICP were present in (n=15) 50% of patients.

In present study of total patients (N=30) only 50% had hormonal symptoms. Acromegaly was present in (N=5) 16.7% patients, Amenorrhea was present in (N=2) 6.7% of patients. Cushing feature was present in (N=3) 10% patients. Hirsutism was present in (N=4) 13.3% patients. Hypothyroidism was present in (N=1) 3.3% patient.

In our study (N=14) 46.7% patients have duration of symptoms < 6 months, 6 months -12 months (N=6) 20%, 1yr-2yr (N=3) 10% & (N=7) 23.3% had duration of symptoms more than 2 yr.

**Visual Acuity**
In our study 6/6 - 6/24 visual acuity was present in 73.3%(N=22) patients, 6/36 - 6/60 visual acuity was present in 13.3%(N=4) patient, Hand movement was present in 6.7%(N=2), perception of light negative in 3.3% (N=1) & perception of light positive in 3.3% (N=1) patients.

**Fundus**
In our study 70%(N=21) had normal fundus, 16.7%(N=5) had pale optic Disc & 13.3%(N=4) had optic atrophy (primary/secondary).

**Visual field**
In our study 43.3%(N=13) patients had bi-temporal hemianopia, Normal field of vision in 33.3%(N=10), Blind 13.3%(N=4), Upper Quadrantanopia was present in 6.7%(N=2) & Total field loss in 3.3%(N=1).

In our study Hydodense lesion was seen in 66.7%(N=20) of patients, hyperdense lesion was seen in 6.7%(N=2) & Heterogenous lesion was seen in 23.3%(N=7). In our study 50%(N=15) were solid lesions, 30%(N=9) were cystic lesions & 20%(N=6) were mixed lesions.

In our study vascular invasion was seen in 26.7%(N=8) of patients.

In our study T1-W image 96.7%(N=29) were hypointense & 3.3%(N=1) were hyperintense & on T2-W image 100%(N=30) were hyperintense. In our study 100%(N=30) were macroadenoma pituitary Tumours. Suprasellar extension was present in 90%(N=27) patients & Vascular invasion seen in 26.7%(N=8) patients.

**DISCUSSION**
Pituitary adenomas can produce visual loss by compression of the optic chiasm or nerves. An extension of >10 mm above the sellar diaphragm is necessary to compress the anterior visual system.[9][10]

Pituitary adenoma can be described as microadenoma, macroadenoma, and giant tumors based on size. Microadenoma is a tumor less than 10 mm, while macroadenoma describes a tumor larger than 10mm. Giant pituitary tumors are bigger than 40 mm.

**Table 1.** Comparison of neurological complaints in various studies

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Study</th>
<th>No. of patients</th>
<th>Visual Impairment (%)</th>
<th>Headache (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Khaled Al dahmani et al (2016)</td>
<td>1005</td>
<td>76</td>
<td>62</td>
</tr>
<tr>
<td>2</td>
<td>Elena Valassi et al (2018)</td>
<td>51</td>
<td>51</td>
<td>34</td>
</tr>
</tbody>
</table>
Visual symptom is one of the major presenting manifestations of a pituitary macroadenoma causing considerable burden to patients and their families [11]. In present study [Table- 1] vision loss (83.3%) was the most common symptoms followed by Headache (80%) and followed by features of raised ICP (50%) which is consistent with most of the studies of Mukerji K K et al[12], Khaled Al dahmani et al[13],Elena Valassi et al(1999)[14], Pamela U Freda et al(1999)[15], Amit Padwal et al (2017)[16] 

Table 2. Comparison of Harmonal symptoms in various studies

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients</th>
<th>Acromegaly</th>
<th>Cushingoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Khaled Al dahmani et al (2016)</td>
<td>1005</td>
<td>6%</td>
<td>0%</td>
</tr>
<tr>
<td>2 Mukherji KK et al (2016)</td>
<td>1007</td>
<td>23.9%</td>
<td>8.6%</td>
</tr>
<tr>
<td>3 Dong Kyulee (2018)</td>
<td>102</td>
<td>18.3%</td>
<td>0%</td>
</tr>
<tr>
<td>4 Present study</td>
<td>30</td>
<td>16.7%</td>
<td>10%</td>
</tr>
</tbody>
</table>

The histologic diversity accounts for its ability to secrete a variety of hormones that include the growth hormone (GH), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin (PRL). The median lobe produces melanocyte-stimulating hormone (MSH). The neurohypophysis is composed of the neural stalk and the neural lobe and functions as the primary storage site for antidiuretic hormone (ADH) and oxytocin (OX). These hormones as well as other biologically active substances are released into the adjacent capillaries in response to hypothalamic nerve impulses [17,18,19]. Hypersecretion of prolactin, growth hormone, ACTH and TSH produces corresponding clinical syndromes [19]. In present study 50%tumours were non functional which was not correlating with Mukherji K K et al [12] were 68.8% were non functioning &Dong Kyu lee [20] were 80% were non functioning tumours.[Table- 2]. In present study 16.7% presented with features of Acromegaly being the most commonest followed by Cushing features in 10% which is consistent with Khaled Al Dahmani et al[13] 6%, Mukherji KK et al[12] 23.9%, Dong Kyu lee [20] 18.3%.

The most common consistent feature of these tumors is visual loss, a consequence of suprasellar growth and compression of anterior visual pathways. An asymmetric bitemporal hemianopia is the classically observed deficit, although other patterns of visual dysfunction commonly occur such as the junctional scotomas, monocular field defects, papilledema, optic atrophy and total blindness[21]. In the present study on fundoscopic Examination (13.3%) patient had optic atrophy as a result of long-standing chiasmal compression from a pituitary macroadenoma.In a study by Dhasmana et al[22] optic atrophy was seen clearly in 17% of patients with pituitary adenomas and all of them had significantly affected vision. Mukherji K K et al [12] study too, had similar percentage (18.2%) of patients presented with optic atrophy and most of the patients had a poor Visual acuity ranging from 6/36 -6/60 to no light perception.[Table- 3]

Table 3. Comparison of Optic Atrophy in various studies

<table>
<thead>
<tr>
<th>S. NO.</th>
<th>Study</th>
<th>Optic Atrophy %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Dhasmana et al (2011)</td>
<td>17</td>
</tr>
<tr>
<td>3.</td>
<td>Present Study</td>
<td>13.3</td>
</tr>
</tbody>
</table>

From the surgical stand point sellar and parasellar masses such as pituitary tumors can be can be classified on the basis of their size and growth characteristics as determined by imaging studies. The most enduring classification is that devised by Hardy and modified by Wilson[23].

<table>
<thead>
<tr>
<th>Grade</th>
<th>Grading</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade-0</td>
<td>Microadenoma&lt;1cm:No sellar changes</td>
</tr>
<tr>
<td>Grade-1</td>
<td>Microadenoma&lt;1cm:Minor sellar changes</td>
</tr>
<tr>
<td>Grade-2</td>
<td>Macroadenoma with diffuse enlargement</td>
</tr>
</tbody>
</table>
Grade-3 Macroadenoma with focal destruction
Grade-4 Macroadenoma with extensive destruction of sella

Extrasellar extension
STAGE-A Extending to suprasellar cistern
STAGE-B Extending to third ventricle floor
STAGE-C Extending into the third ventricle
STAGE-D Extensive lateral intradural extension
STAGE-E Extensive lateral extradural extension.

KNOSP Classification

CT is better than MR imaging for detecting calcifications, and can be used complementary to MR imaging if a primary bony lesion is suspected (e.g., chordoma, chondrosarcoma) and also in defining the sphenoid sinus anatomy if endonasal/sublabial endoscopic or microscopic transphenoidal approach is planned [27,28]. CT scan is also beneficial in detecting pituitary apoplexy which will have a hyperdense appearance.

In our study, 29 cases showed hypointensity on T1 Weighted image, while one case showed hyperintensity. All cases showed hyperintensity on T2 weighted image. These MRI Finding are supported by most of other studies, like Pratisruti Hui et al[29] & Kushak Gehlot et al [30], where similar results were obtained. [Table- 5]

<table>
<thead>
<tr>
<th>Study</th>
<th>T1 MRI</th>
<th>T2 MRI</th>
<th>Contrast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kushak Gehlot et al (2019)</td>
<td>Hypointense - 84% Hyperintense- 9.2%</td>
<td>Hyperintensity -80%</td>
<td>75.9%</td>
</tr>
<tr>
<td>Pratisruti Hui et al (2019)</td>
<td>Hypointense -100%</td>
<td>Hyperintensity -86%</td>
<td>92%</td>
</tr>
<tr>
<td>Present study</td>
<td>Hypointense - 84% Hyperintense- 9.2%</td>
<td>Hyperintensity -100%</td>
<td>80%</td>
</tr>
</tbody>
</table>

Post-operative visual Recovery played a significant role, post-operative assessment was done immediately post-operative, after 1 month & after 3 month of surgery. Most of the patients showed visual recovery after 3 month. A Ashish Suri et al [31] showed visual improvement in 30% patients, Apjit Kaur et al [32] showed visual improvement in 44.8%, Mukherji K K et al [12] showed improvement in 71.1% cases at 3 months which is similar to our study of 83.3% [Table-6].

<table>
<thead>
<tr>
<th>Study</th>
<th>Post-op Visual recovery %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashish Suri et al (2008)</td>
<td>30%</td>
</tr>
<tr>
<td>Apjit Kaur et al</td>
<td>44.8%</td>
</tr>
<tr>
<td>Mukherji K K et al (2016)</td>
<td>71.1%</td>
</tr>
<tr>
<td>Our study</td>
<td>83.3%</td>
</tr>
</tbody>
</table>

The minimally invasive transsphenoidal approach can be used effectively for 95% of pituitary tumors.
Exceptions are those large tumors with significant temporal or anterior cranial fossa extension. In such circumstances, transcranial approaches are often more appropriate. Occasionally, combined transsphenoidal and transcranial approaches are used. Nevertheless, some surgeons extend the basic transsphenoidal exposure in order to remove some of these tumors and avoid a craniotomy [33,34]

CONCLUSION

Good results are seen in patients who have lesser duration of symptoms, good pre-operative Visual Acuity have improved final Visual outcome. In our study most cases of pituitary adenoma were functional, so patients with pituitary prolactinoma showed better visual recovery. Post-operative visual recovery is most promising after 3 months to 1 year of surgery. immediate results of visual recovery should not be expected. most of patients presented with larger adenomas with supra-sellar & parasellar extension with encasement of internal carotid artery had poor Visual recovery as compared to small adenomas. Patients who underwent Endoscopic Trans-nasal, trans-sphenoidal resection had better post-operative recovery with less patient morbidity & less post-operative complications and lesser duration of post-operative hospital stay.

REFERENCES

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