Frequency of Pituitary Adenoma among the Patients with Chronic Headache

Asadullah Jatoi a*, Asma Jatoi b, Noman Ahmed Shaikh a, Ashok Kumar Narsani a and Mona Liza Mahesar a

a Institute of Ophthalmology, Liaquat University of Medical and Health Sciences, Jamshoro, Sindh, Pakistan.

b Department of Radiology, Liaquat University of Medical and Health Sciences, Jamshoro, Sindh, Pakistan.

Authors’ contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

ABSTRACT

Background: Antero-superior, Pituitary Gland lies in vicinity of optic chiasm and antero-inferiorly, it is related with posterior wall of sphenoid bone. Pituitary Gland is consisting of three lobes: Anterior, intermediate and posterior and their secretion are regulated by hypothalamus.

Aims and Objectives: To identify pituitary adenoma in the patients coming with complain of chronic headache.

Materials and Methods: Seven hundred sixty-four patients were included in our study. All the patients with chronic headache with/without decreased vision and visual field defects were included our study. Those patients already diagnosed with any other cause of headache such as uncontrolled blood pressure, tumor or diagnosed case of pituitary adenoma and patient with glaucoma were excluded. Detailed history was taken and ocular examination was done. MRI orbit and brain with contrast was done in all patients.

Results: Out of 764 patients, 32 patients were diagnosed as having pituitary adenoma. Macro-adenoma was present in 30 patients and micro-adenoma in 2 patients. On MRI majority of patients had optic chiasm compression with bi-temporal hemianopia.

Conclusion: All the patients with chronic headache with/without visual disturbances and visual field defect must be properly examined and investigated as that will help other researchers to diagnose the Pituitary Adenomas.
Keywords: Chronic headache; vision; visual field defect; pituitary adenoma.

1. INTRODUCTION

The hypophysis cerebri or pituitary gland (PG), also known as Master Gland, is an ovoid shaped structure, measuring about 0.8 cm from front to back and 1.2 cm diagonally and weighing about 0.5 kg. [1,2] The pituitary fossa or Sella turcica of sphenoid bone, a cup shaped depression contains the PG and the fossa is bounded by diaphragma sellae (dura) superiorly. Anterior-superior, PG lies in vicinity of optic chiasm and antero-inferiorly, it is related with posterior wall of sphenoid bone [2,3]. PG is consisting of three lobes: Anterior, intermediate and posterior and their secretion is regulated by hypothalamus [4]. Anterior pituitary gland (APG) or adenohypophysis secretes growth hormones (GH), adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH) and luteinizing hormone (LH), and produce prolactin (PRL) and their secretion is controlled by hypothalamus through secretion of somatostatin and dopamine [5,6]. Posterior pituitary gland (PPG) stores and secretes Antidiuretic hormone (ADH) and oxytocin, which are formed in hypothalamus. [7,8] Pituitary Adenomas (PAs) are compendium of tumors arising from APG and it accounts for 10-25 % of tumors, out of all intracranial tumors [9,10]. Prevalence of pituitary adenoma is 17% worldwide. PG tumors classification has been given by world health organization (WHO) (Fig no 1). [11] PAs historically has also been defined according to their size i.e., Microadenoma if less than 1 cm or Macroadenoma if equal or more than 1 cm and if size is more than 4 cm it is termed as Giant Pituitary Adenoma [12]. PAs can be categorized into functional and non-functional. Functional Pituitary adenoma (FPAs) includes GH tumors, gonadotropin secreting tumors, prolactinomas, thyroid hormone tumors, adrenocorticotropic hormone tumors and multihormone tumors. They are treated due to symptoms produced due to excessive hormonal secretion. Whereas in Non-Functional Pituitary adenoma (NFPAs), there is no excessive secretion of hormones, they mainly represent with effect of local pressure such as headache, visual disturbances [13]. Majority of PAs are benign. Patients with PAs comes with complaint regarding to tumor endocrine related problems or secondary to tumor space occupying symptoms such chronic headache of varying intensity and gradual blurring or loss of vision [14]. Optic chiasm is damaged by pituitary adenoma due to direct compaction or due to alteration of vascular supply by tumor. Patient presents with chronic headache and visual symptoms such as decreased visual acuity, visual field and color vision defects, primary optic atrophy and third nerve abnormalities [15]. Magnetic Resonance Imaging (MRI) is best diagnostic imaging modality for diagnosis of PAs [16]. For PAs, trans-sphenoid surgery in starting, followed by pharmacological treatment if it is not resolved by surgical treatment. Surgical option is considered as first line of treatment option except for prolactinomas for which initial therapy is medical regimen [17].

2. MATERIALS AND METHODS

This was two-year study, conducted from first January 2019 to thirty first December 2020, at Institute of Ophthalmology (IOL) at Liaquat University of Medical Health Sciences (LUMHS). Seven hundred sixty-four patients were enlisted in our study. All the patients with chronic headache with/without decreased vision and/or visual field defects were included in this study. Those patients already diagnosed of any other cause of headache such as raised blood pressure, tumor, or already diagnosed case of pituitary adenoma were excluded from our study and patient with diagnosed case of glaucoma with glaucomatous cupping were also excluded. Detailed history regarding ocular and systemic symptoms was taken from patients. In all patients, best corrected visual acuity (BCVA) was checked through Log MAR chart, pupillary examination and color vision test was done, intracocular pressure (IOP) was checked with Goldman’s tonometer and anterior and posterior segment examination was done through slit lamp with 78 D lens. Visual field testing was done through confrontation test and Haag Streit Octopus Perimeter in all patients. Fundus photography was also done. All patient included in this study had their MRI brain and orbit with contrast done. Through MRI, location of tumor was categorized as having suprasellar &/ Parasellar extension. Optic chiasm and/or optic nerve compression was noted on MRI. Antero-posterior, craniocaudal and transverse size of tumor was measured on MRI. Whether PAs are functional or non-functional, pituitary hormones were investigated.

3. RESULTS

Total number of patients was 764. Out of 764, 32 patients were diagnosed as pituitary adenoma. In
32 patients. Age ranges from 25 years to 62 years and median age is 37.25. (Tables 1 and 2) Out of 32 patients, 12 were females and 20 were males (Table 3).

### Table 1. Statistical range of Age of study subjects

| Age     | Range: 25-62 | Median: 37.25 | SD: 12.87 |
|---------|--------------|---------------|-----------|

Most common symptom in patients diagnosed with pituitary adenoma was headache (100%), blurred or loss of vision (87.5%), nausea and vomiting (43.75%), amenorrhea (15.63%) and gynecomastia (6.25%) in patients (Table 4).

Optic nerve compression was seen on MRI in 93.75% cases (Table 5).

Supra-seller and para-seller extension of pituitary tumor was also seen on MRI brain and orbit. (Table 6).

Out of 32 patients, diagnosed with Pituitary adenoma, 30 were macroadenoma and 2 were microadenoma (Table 7).

| Pituitary adenomas                    | Somatotroph adenoma |
|--------------------------------------|---------------------|
|                                      | Lactotroph adenoma  |
|                                      | Thyrotroph adenoma  |
|                                      | Corticotroph adenoma|
|                                      | Gonadotroph adenoma |
|                                      | Null-cell adenoma   |
|                                      | Plurihormonal and double adenomas |

| Pituitary carcinoma                  | Pitucytoma          |
|--------------------------------------|---------------------|
| Pituitary blastoma                   | Granular cell tumor of the sella |
|                                      | Spindle cell oncocytoma |
|                                      | Sellar ependymoma    |

| Neuronal and paraneuronal tumors     | Gangliocytoma and mixed gangliocytoma-adenom |
|--------------------------------------|-----------------------------------------------|
|                                      | Neurocytoma                                   |
|                                      | Paraganglioma                                  |
|                                      | Neuroblastoma                                 |

| Craniopharyngioma                    | Adenomatous craniopharyngioma                  |
|--------------------------------------|-----------------------------------------------|
|                                      | Papillary craniopharyngioma                    |

| Mesenchymal and stromal tumors       | Meningioma                                     |
|--------------------------------------|-----------------------------------------------|
|                                      | Schwannoma                                     |
|                                      | Chordoma, NOS                                  |
|                                      | Chondroid chordoma                             |
|                                      | “Dedifferentiated” chordoma                    |
|                                      | Solitary fibrous tumor/hemangiopericytoma      |
|                                      | Grade 1 SFT/HPC                                |
|                                      | Grade 2 SFT/HPC                                |
|                                      | Grade 3 SFT/HPC                                |

| Hematolymphoid tumors                | Germinoma                                       |
|--------------------------------------|------------------------------------------------|
| Germ cell tumors                     | Yolk sac tumor                                  |
|                                      | Embryonal carcinoma                             |
|                                      | Choriocarcinoma                                 |
|                                      | Teratoma, NOS                                   |
|                                      | Mature teratoma                                 |
|                                      | Immature teratoma                               |
|                                      | Teratoma with malignant transformation          |
|                                      | Mixed germ cell tumor                           |

Secondary tumors

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**Fig. 1. WHO pituitary tumor classification**
Table 2. Age wise distribution of participants

| Age       | Male | Female |
|-----------|------|--------|
| 0-20      | 0    | 0      |
| 21-40     | 14   | 10     |
| 41-60     | 2    | 2      |
| 61 and above | 4  | 0      |
| Mean      | 40.5 | 27.5   |

Table 3. Gender distribution

| Gender | Number |
|--------|--------|
| Male   | 20     |
| Female | 12     |

Table 4. Symptoms observed by participants

| Symptoms                        | Number | Percentage |
|---------------------------------|--------|------------|
| Headache                        | 32     | 100 %      |
| Loss of vision                  | 28     | 87.5 %     |
| Nausea and vomiting             | 14     | 43.75 %    |
| Gynecomastia                    | 2      | 6.25 %     |
| Amenorrhea                      | 3      | 9.38 %     |

Table 5. Optic chiasm compression by Pituitary adenoma

| Optic chiasm compression | Number | Percentage |
|--------------------------|--------|------------|
| Present                  | 30     | 93.75 %    |
| Absent                   | 2      | 6.25 %     |

Table 6. Tumor extension

| Tumor extension | Number | Percentage |
|-----------------|--------|------------|
| Suprasellar     | 30     | 93.75 %    |
| Parasellar      | 28     | 87.5 %     |

Table 7. Type of pituitary adenoma

| Type of pituitary adenoma | N(%)  |
|---------------------------|-------|
| Macroadenoma              | 30 (93.75%) |
| Microadenoma              | 2 (6.25%)  |

Visual field defects were recorded on Haag Streit Octopus. Bitemporal hemianopia (visual field defect type 1) was seen in 23 patients, temporal hemianopia in one eye with complete visual field loss in fellow eye is seen in 3 patients (visual field defect type 2). In two patient lower temporal defects were seen (visual field defect type 3). In 2 patients, temporal hemianopia was seen in one eye and lower temporal defect was seen in fellow eye (type 4 visual field defect) (Table 8).

Tumor size is depicted in Table 9.

All patients presented with visual loss of variable degree. (Table 10) Most of patients presented with vision of 6/36 or less (34.38%).

4. DISCUSSION

About 15% of brain tumors are pituitary tumors. They grow, enlarge and compress the optic chiasm fibers superiorly which causes visual field defects particularly bitemporal hemianopia, gradual visual loss, color abnormalities and optic disc atrophy. Thus, major indication of pituitary gland tumor surgery is visual problems. [18-20]. In the current study, median age was 37.25 years, ranging from 25 years to 62 years, which is quite similar to age of presentation seen in other studies such as study done by Setyowati R. which showed patients were between the age of 29-65 years [21]. Mansour AA et al., reported median age of 38.2 years ±15 [22]. In our study,
Table 8. Visual field defects observed among the participants

| Types of visual field defects | N(%)       |
|------------------------------|------------|
| Type 1                       | 23 (71.87%)|
| Type 2                       | 3 (9.38%)  |
| Type 3                       | 2 (3.12%)  |
| Type 4                       | 2 (3.12%)  |
| Normal                       | 2 (3.12%)  |

Table 9. Tumor size among the study subjects

| Tumor size | Antero-posterior | Craniocaudal | Transverse |
|------------|------------------|--------------|------------|
| Range      | 1.5-5 cm         | 1.5-4.8 cm   | 1.9-4 cm   |
| Median     | 2.93 cm          | 5.48 cm      | 2.75 cm    |
| SD         | 1.4              | 2.48         | 1.97       |

Table 10. Visual Acuity observed among the study subjects

| Visual acuity | Right eye | Left eye |
|---------------|-----------|----------|
| 6/9 or 6/6    | 3 (9.38%) | 0        |
| 6/12          | 1 (3.12%) | 6 (18.75%)|
| 6/18          | 2 (6.25%) | 0        |
| 6/24          | 1 (3.12%) | 5 (15.63%)|
| 6/36          | 11 (34.38%)| 11 (34.38%)|
| 6/60          | 11 (34.38%)| 4 (12.5%)  |
| Less than 6/60| 3 (9.38%) | 6 (18.75%)|

there was male predominance of 68.75%. This can be due to fact that patients reported to us were mainly due to headache and decreased vision rather than any hormonal issue secondary to macroadenoma, similar to study conducted by Rehman L. which showed 63.5% patients were males [23]. Headache and visual disturbance are reported to be most common symptom in patients having pituitary adenoma. In general population, prevalence of headache is about 50% and in patients having pituitary adenoma it ranges from 37.5-70%. All patients, with complain of chronic headache of varying intensity were included in this study. Rehman L. also reported headache and visual disturbance to be present in 87.3% and 88.8% of patients respectively, in his study. [23-26]. Visual field defects associated with pituitary adenoma ranges from 37-96%. [27]. Lee JP et al., reported that 74 % of patients had visual field defect due to pituitary adenoma, out of which temporal visual field defect was commonly present in 56% cases. [28]. In our study, visual field defect was present in 93.75% of patients with bitemporal visual field defect was commonly present in 71.87 %. In our study, suprasellar and Parasellar extension was seen in 93.75 % and 87.5% cases respectively causing optic chiasm compression. Suprasellar and Parasellar extension was common as macroadenoma was common in our study. Gupta K. also reported that majority of macroadenoma's had supra sellar extension (72.7%). [29]. Limitation of our study was that number of patients was less. The patients were sent to neurosurgical department for evaluation and treatment but the follow-up regarding management was difficult and cannot be done.

5. CONCLUSION

Pituitary adenoma is one of the common causes of headache. Patients with pituitary adenoma particularly do not have ocular symptoms initially. So chronic headache is considered as major symptom for its diagnosis particularly when there is macroadenoma as it occurs in our study.

CONSENT

As per international standard or university standard, patients’ written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).
COMPETING INTERESTS

Authors have declared that no competing interests exist.

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