

Original Research Article

FREQUENCY OF PITUITARY ADENOMA AMONG THE PATIENTS WITH CHRONIC HEADACHE

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.

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. Antero-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), adrenocorticotrophic 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) (Figure 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, gonadotropic hormones tumors, prolactinomas, thyroid hormone tumors, adrenocorticotrophic hormone tumors and multihormone tumors. They are treated due to symptoms produced due to excessive hormonal secretions. 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 complain 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]

Figure No 1: WHO pituitary tumor classification

Pituitary adenomas	Somatotroph adenoma Lactotroph adenoma Thyrotroph adenoma Corticotroph adenoma Gonadotroph adenoma Null-cell adenoma Plurihormonal and double adenomas
Pituitary carcinoma Pituitary blastoma Tumors of the posterior pituitary	Pituicytoma Granular cell tumor of the sella Spindle cell oncocytoma Sellar ependymoma
Neuronal and paraneuronal tumors	Gangliocytoma and mixed gangliocytoma-adenoma Neurocytoma Paraganglioma Neuroblastoma
Craniopharyngioma	Adamantinomatous 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 Germ cell tumors	Germinoma Yolk sac tumor Embryonal carcinoma Choriocarcinoma Teratoma, NOS Mature teratoma Immature teratoma Teratoma with malignant transformation Mixed germ cell tumor
Secondary tumors	

MATERIAL AND METHOD:

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, intraocular 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.

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. (Table 1 and 2) Out of 32 patients, 12 were females and 20 were males. (Table No 3)

Table no 1: Statistical range of Age of study subjects

Age	Range: 25-62 Median: 37.25 SD: 12.87
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Table No 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 No 3: Gender distribution

Male	20
Female	12

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 no 4)

Table No 4: Symptoms observed by participants

SYMPTOMS	NUMBER	PERCENTAGE
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Headache	32	100 %
Loss of vision	28	87.5 %
Nausea and vomiting	14	43.75 %
Gynecomastia	2	6.25 %
Amenorrhea	3	9.38 %

Optic nerve compression was seen on MRI in 93.75% cases. (Table No 5)

Table No 5: Optic chiasm compression by Pituitary adenoma

OPTIC CHIASM COMPRESSION	NUMBER	PERCENTAGE
Present	30	93.75 %
Absent	2	6.25 %

Supra-sellar and para-sellar extension of pituitary tumor was also seen on MRI brain and orbit. (Table No 6)

Table No 6: Tumor extension

TUMOR EXTENSION	NUMBER	PERCENTAGE
Suprasellar	30	93.75 %
Parasellar	28	87.5 %

Out of 32 patients, diagnosed with Pituitary adenoma, 30 were macroadenoma and 2 were microadenoma. (Table no 7)

Table No 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 No 8)

Table no 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%)

Tumor size is depicted in table No 9.

Table No 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

All patients presented with visual loss of variable degree. (Table No 10) Most of patients presented with vision of 6/36 or less (34.38%).

Table No 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%)

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 \pm 15. [22] In our study, 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.

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.

Ethical Approval:

As per international standard or university standard ethical approval has been collected and preserved by the authors.

REFERENCES:

1. Barkhoudarian G, Kelly DF. *The Pituitary Gland: Anatomy, Physiology, and its Function as the Master Gland. In Cushing's Disease 2017 Jan 1 (pp. 1-41). Academic Press.*
2. Larkin S, Ansorge O. *Development and microscopic anatomy of the pituitary gland.*
3. Varrassi M, Bellisari FC, Bruno F, Palumbo P, Natella R, Maggialetti N, De Filippo M, Di Cesare E, Barile A, Masciocchi C, Caranci F. *High-resolution*

- magnetic resonance imaging at 3T of pituitary gland: advantages and pitfalls. *Gland surgery*. 2019 Sep;8(Suppl 3):S208.
4. El Sayed SA, Fahmy MW, Schwartz J. *Physiology, pituitary gland*. StatPearls [Internet]. 2020 Jun 1.
 5. Rawindraraj AD, Basit H, Jialal I. *Physiology, Anterior Pituitary*. StatPearls [Internet]. 2020 Jun 1.
 6. Patel H, Tiwari V. *Physiology, Posterior Pituitary*.
 7. Asioli S, Righi A, Iommi M, Baldovini C, Ambrosi F, Guaraldi F, Zoli M, Mazzatenta D, Faustini-Fustini M, Rucci P, Giannini C. Validation of a clinicopathological score for the prediction of post-surgical evolution of pituitary adenoma: retrospective analysis on 566 patients from a tertiary care centre. *European journal of endocrinology*. 2019 Feb 1;180(2):127-34.
 8. Qian Y, Qiu Y, Li CC, Wang ZY, Cao BW, Huang HX, Ni YH, Chen LL, Sun JY. A novel diagnostic method for pituitary adenoma based on magnetic resonance imaging using a convolutional neural network. *Pituitary*. 2020 Feb 15:1-7.
 9. Inoshita N, Nishioka H. The 2017 WHO classification of pituitary adenoma: overview and comments. *Brain tumor pathology*. 2018 Apr;35(2):51-6.
 10. Donovan LE, Welch MR. Headaches in patients with pituitary tumors: a clinical conundrum. *Current pain and headache reports*. 2018 Aug;22(8):1-7.
 11. https://eyewiki.aao.org/Pituitary_Adenoma
 12. Inder WJ, Jang C. Pituitary disease: An update. *Pituitary*. 2021 Jan;50(1-2).
 13. Qin J, Li K, Wang X, Bao Y. A comparative study of functioning and non-functioning pituitary adenomas. *Medicine*. 2021 Apr 9;100(14).
 14. Yang Q, Li X. Molecular network basis of invasive pituitary adenoma: a review. *Frontiers in endocrinology*. 2019 Jan 24;10:7.
 15. Sun M, Zhang ZQ, Ma CY, Chen SH, Chen XJ. Predictive factors of visual function recovery after pituitary adenoma resection: a literature review and meta-analysis. *International journal of ophthalmology*. 2017;10(11):1742.
 16. Iglesias P, Arcano K, Triviño V, García-Sancho P, Díez JJ, Villabona C, Cordido F. Prevalence, clinical features, and natural history of incidental clinically non-functioning pituitary adenomas. *Hormone and Metabolic Research*. 2017 Jul 31;49(9):654-9.
 17. Molitch ME. Diagnosis and treatment of pituitary adenomas: a review. *Jama*. 2017 Feb 7;317(5):516-24.
 18. Park SH, Kang MS, Kim SY, Lee JE, Shin JH, Choi H, Kim SJ. Analysis of factors affecting visual field recovery following surgery for pituitary adenoma. *International Ophthalmology*. 2021 Feb 24:1-8.
 19. Das B, Batool S, Khoja A, Islam N. Presentation, Management, and Outcomes of Nonfunctioning Pituitary Adenomas: An Experience from a Developing Country. *Cureus*. 2019 Sep;11(9).
 20. Würth R, Thellung S, Corsaro A, Barbieri F, Florio T. Experimental evidence and clinical implications of pituitary adenoma stem cells. *Frontiers in endocrinology*. 2020;11.
 21. Setyowati R, Wicaksono AS, Hartanto RA, Mahayana IT, Prawiroranu S. Visual Finding in Patient with Pituitary Macroadenoma underwent Transphenoid Surgery. *Ophthalmologica Indonesiana*. 2019 Aug 28;45(2):76-.
 22. Mansour AA, Alhamza AH, Almomin AM, Zaboon IA, Alibrahim NT, Hussein RN, Kadhim MB, Alidrisi HA, Nwayyir HA, Mohammed AG, Al-Waeli DK. Spectrum of Pituitary disorders: A retrospective study from Basrah, Iraq. *F1000Research*. 2018;7.

23. Rehman L, Rehman UL, Jabeen R, Rizvi R. Endoscopic Trans-Sphenoidal surgery; Efficacy and response in Pituitary Adenoma. *Pakistan journal of medical sciences*. 2018 Mar;34(2):412.
24. Donovan LE, Welch MR. Headaches in patients with pituitary tumors: a clinical conundrum. *Current pain and headache reports*. 2018 Aug;22(8):1-7.
25. Lake MG, Krook LS, Cruz SV. Pituitary adenomas: an overview. *American family physician*. 2013 Sep 1;88(5):319-27.
26. Wang SJ, Hung CW, Fuh JL, Lirng JF, Hwu CM. Cranial autonomic symptoms in patients with pituitary adenoma presenting with headaches. *Acta Neurol Taiwan*. 2009 Jun 1;18(2):104-2.
27. Dhasmana R, Nagpal RC, Sharma R, Bansal KK, Bahadur H. Visual fields at presentation and after trans-sphenoidal resection of pituitary adenomas. *Journal of ophthalmic & vision research*. 2011 Jul;6(3):187.
28. Lee JP, Park IW, Chung YS. The volume of tumor mass and visual field defect in patients with pituitary macroadenoma. *Korean journal of ophthalmology: KJO*. 2011 Feb;25(1):37.
29. Gupta K, Sahni S, Sagar K, Vashisht G. Evaluation of clinical and magnetic resonance imaging profile of pituitary macroadenoma: A prospective study. *Journal of natural science, biology, and medicine*. 2018 Jan;9(1):34.