International Journal of Research in Medical Sciences
Tali TA et al. Int J Res Med Sci. 2023 Jun;11(6):2181-2185
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20231639

Original Research Article

Clinico-epidemiological profile and treatment outcome of pituitary adenomas: a retrospective study

Tavseef Ahmad Tali[1], Fiza Amin[2], Shahid Rashid Sofi[1]*, Nazir Ahmad Khan[1], Javaid Ahmad Dar[3], Mushtaq Ahmad Sofi[1]

[1]Department of Radiation Oncology, Sher-I-Kashmir Institute of Medical Sciences, Srinagar, Jammu & Kashmir, India
[2]Department of Gynaecology and Obstetrics, Skims Medical College and Hospital, Srinagar, Jammu & Kashmir, India
[3]Department of Cardiology, Christian Medical College, Vellore, Tamil Nadu, India

Received: 12 April 2023
Revised: 11 May 2023
Accepted: 17 May 2023

***Correspondence:**
Dr. Shahid Rashid Sofi,
E-mail: rashidshahid853@gmail.com

ABSTRACT

Background: Aim of this study was to evaluate the clinico-epidemiological profile and treatment outcome of pituitary adenomas.
Methods: This was a retrospective study performed in the department of Radiation Oncology, Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, India, in which 30 cases diagnosed with pituitary adenoma from January 2016 to December 2021 were studied. There clinical and epidemiological features, treatment, overall survival and follow-up data was analyzed.
Results: Most patients were female in gender 17 (57%), and the incidence rate was higher in female patients than male. Microadenoma was seen in just 4 (13%) patients. Macroadenoma in 12 (40%) and giant tumours in 14 (47%). At three and five years, the overall survival rate was 92% and 83%, respectively. Additionally, patients who got adjuvant radiation had a higher overall survival rate (84% versus 76%, p=.833) than those who did not.
Conclusions: Radiotherapy is an effective treatment for pituitary adenomas, able to achieve excellent disease control. Patients with pituitary adenomas should be identified at an early stage so that effective treatment can be implemented. Initial therapy is generally transsphenoidal surgery with irradiation reserved for patients who do not achieve adequate reduction in tumor size after surgery.

Keywords: Epidemiology, Overall survival, Pituitary adenoma, Radiotherapy

INTRODUCTION

Anterior pituitary tumours are called pituitary adenomas. Most pituitary tumors are slow-growing and benign. They are classed according on their size or cell of origin. Pituitary adenomas are categorised as microadenomas, macroadenomas, or big tumours based on their size. There are active pituitary adenomas, and the cells that make them up boost the anterior pituitary's hormone output of one or more hormones. As an alternative, there are non-functioning adenomas that do not secrete hormones but may compress the anterior pituitary's surrounding tissue, resulting in hormonal imbalances. Pituitary adenomas in families account for 5% of all pituitary tumours.[1]

Most pituitary adenomas are discovered by chance when imaging techniques are used for other purposes. It is difficult to determine with precision the prevalence of pituitary adenomas in the general population due to its

sneaky nature, modest size, and incidental diagnosis. Based on autopsy and radiographic data, the expected prevalence of pituitary adenomas is extrapolated. There is a wide range of prevalence among studies and the source of information.[2] In a meta-analysis, the pituitary adenomas frequency was 16.7% average; in autopsies 14.4% and in radiology tests 22.5%.[3] The most popular study from Iceland showed a prevalence of 115 per 100,000 population. [2,4-6]

Transsphenoidal surgical adenoma resection is the initial treatment chosen. Rarely is craniotomy performed.[7,8] With expert pituitary surgeons, remission rates can be achieved in 80% to 90% of patients with microadenomas and 40% to 70% of those with macroadenomas, with a 10% to 20% recurrence rate because of regrowth of tumor remnants over several years.[8] With more experience as a neurosurgeon, complication rates drop, and they are roughly 0.4% for carotid artery injury, 0.6% for central nervous system injury, 0.5% for vision loss, 0.4% for ophthalmoplegia, 1.5% for cerebrospinal fluid leak, 0.5% for meningitis, 7.2% for hypopituitarism, 7.6% for diabetes insipidus, and 0.2% for death.[9,10] Even with experienced neurosurgeons, delayed hyponatremia occurring 7 to 10 days postoperatively can occur in 4% to 10% of patients due to inappropriate vasopressin secretion.[11]

Irradiation is reserved for patients who do not achieve adequate reduction in tumor size, hormone levels, or both in response to surgery, medical therapy, or both. The older conventional fractionated therapy has largely been abandoned in favour of giving high-dose irradiation in a single visit or a few visits after careful stereotactic mapping of the tumor, except in the case of large, invasive tumors or those in close proximity to the optic chiasm. Stereotactic radiotherapy results in overall faster reduction in hormone secretion and fewer adverse effects than conventional radiotherapy, although the risk for hypopituitarism remains high for both types of radiotherapy, reaching 20% by 5 years and 80% by 10 to 15 years.[12,13] In this study, we discovered that external beam radiotherapy is a successful medication for pituitary adenomas that are not surgically healed and have residual or recurring diseases, giving long-term local control. In our study, we have studied the role of radiation therapy in recurrent, significant residual disease, post-surgery, and unresectable pituitary adenomas. Although, radiation therapy is not the mainstay treatment for pituitary adenomas but can be used in recurrent and unresectable pituitary adenomas and has shown some survival benefits and decreased the risk of local recurrences.[14] The main objective of this study was to study the clinico-epidemiological profile and treatment outcome of pituitary adenomas.

METHODS

This was a retrospective study performed in the department of Radiation Oncology, Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, India. All necessary clinical and epidemiological details of the 30 cases diagnosed with pituitary adenoma from January 2016 to December 2021 were retrieved. Clinical and epidemiological features, treatment, overall survival and follow-up data were analyzed. These are the following criteria to be eligible for the enrolment as our study participants: a) All the cases of pituitary adenoma who were registered during the study period in our hospital. b) Patients who defaulted or did not complete the treatment for any other medical or natural cause were excluded.

Statistical analysis

Data analysis was done on an MS Windows-based computer. The data were first keyed into a Microsoft Excel spread sheet and cleaned for any in accuracies. Statistical analysis was done using IBM SPSS Statistics for Windows from IBM Corp. (released 2020, Version 27.0. Armonk, NY, USA). Descriptive statistics were used to show categorical variables were shown in the form of frequencies and percentages (mean, standard deviation, percentage). Kaplan Meier survival was used to calculate overall survival, 3 years overall survival and 5 years overall survival. All values were discussed at 5% level of significance. The study was carried out in accordance with the institutional ethics committees (IEC) of SKIMS and the updated Helsinki Declaration from 1964. Informed consent was waived, as this was a retrospective audit of the health records.

RESULTS

In the current study a total of 30 patients were analyzed. Mean age of diagnosis was 49 years, with age ranging from 23 to 65 years. Most patients were female in gender 17 (57%), and the incidence rate was higher in female patients than male. When adjusted for corresponding age groups and sex, a bimodal age-related distribution was observed in female patients, with a first peak seen in adults aged 25-35 years and a second peak in the elderly aged 55-65 years. A unimodal age-related distribution was seen in males and the incidence rate was notably higher in the fifth decade of lifespan.

Most of the patients i.e., 17 (57%) received surgery as their sole treatment modality. Additionally, 13 patients (43%) received radiation therapy as an adjuvant treatment in view of residual diseases after undergoing primary surgical resection with intensity modulated radiation therapy (IMRT) technique to a dose of 54Gy in 30 fractions @ 1.8Gy per fraction over a period of 6 weeks. Diminished vision and headache were the most common presenting symptoms. Microadenoma was seen in just 4 (13%) patients. Macroadenoma in 12 (40%) and giant tumours in 14 (47%). At three and five years, the overall survival rate was 92% and 83%, respectively. Additionally, patients who got adjuvant radiation had a higher overall survival rate (84% versus 76%, p=.830) than those who did not. Older age at diagnosis and larger

tumour size were associated with significantly worse survival compared to younger patients and patients with relatively smaller tumour sizes (Table 1, 2, 3, 4). Acromegaly, Cushing's syndrome, pituitary apoplexy, central diabetes insipidus were the associated abnormalities in these patients.

Table 1: Clinical and demographic profile.

Parameters	Category	n	%
Age	<50 years	20	67
	>50 years	10	33
Gender	Male	13	43
	Female	17	57
Tumour size	Micro adenoma <10mm	4	13
	Macro adenoma >10mm	12	40
	Giant tumour >40mm	14	47
Primary treatment	Surgical resection	30	100
Adjuvant radiotherapy	Received	13	43
	Not received	17	57
Overall survival	3years	5years	
%	92%	83%	

Table 2: Mean 3years overall survival (months).

Mean			
Estimate	**Std. error**	**95% Confidence interval**	
		Lower bound	**Upper bound**
35.204	1.228	32.797	37.610

Table 3: Mean 5year overall survival (months).

Mean			
Estimate	**Std. error**	**95% Confidence interval**	
		Lower bound	**Upper bound**
33.00	1.649	29.769	36.231

Table 4: Mean overall survival (months) in adjuvant radiotherapy.

Adjuvant radiotherapy	Mean			
	Estimate	**Std. error**	**95% confidence interval**	
			Lower bound	**Upper bound**
Yes	32.353	2.033	28.369	36.337
No	29.462	2.304	24.945	33.978
Overall	32.333	1.711	28.980	35.687
Log rank (mantel-cox): chi-square=.046 p=0.830				

DISCUSSION

Although genetic mutations are associated with some tumor types, the pathogenesis of more than 95% of tumors is still unknown. As more mutations are identified along with a better understanding of tumorigenesis, additional medical treatments may be developed targeting specific stages of tumor development. Although a number of medical treatments have been developed for many of the adenomas, there are very few head-to-head comparisons of therapeutic efficacy in randomized clinical trials and such trials are needed. Transsphenoidal selective adenoma resection by an expert pituitary neurosurgeon is recommended as the initial treatment.[15-17] For patients in remission following surgery, continued surveillance with MRI scans and hormone levels should be carried out to detect tumor recurrence or regrowth for up to 20 years following surgery. For those not in remission after surgery, medical therapies should be prescribed that are directed at the tumor, the major target organ (the adrenal gland in Cushing disease), or at hormone receptors that are specific to the tumor type. Irradiation should be reserved for patients whose tumors, hormone levels, or both are not controlled by surgery and medical treatment.[15-18]

Prior cross-sectional observation studies carried outside the United States identified a standardized incidence rate ranging from 0.6 to 7.4 cases per 100,000 inhabitants per year.[19-21] The rising incidence might be related to the significant advancements in neuroimaging, a higher incidentally discovered rate or the increased awareness of pituitary diseases among physicians. Of note, there has been debate about whether the real incidence of pituitary tumor is rising or just the incidentally discovered rate. Raappana et al.[20] demonstrated in their 16-year period study in Northern Finland that the increase in the incidence rate was caused by incidentaloma rather than symptomatic pituitary adenoma, while Radhakrishnan et al discovered that the incidence of symptomatic pituitary tumors also remarkably risen in the Minnesota population varied by age group and patients.[22] Since older patients are more vulnerable to surgery-related complications such as hypopituitarism, cerebrospinal fluid leaks, and diabetes insipidus it is understandable that a wait-and-see protocol was more preferable in some cases.[23.24] Because of the benign histopathological nature of primary pituitary tumors, the prognosis is excellent as far as overall survival. Nevertheless, pituitary tumors are associated with a substantially decreased overall survival, with a mortality rate two to fivefold higher than that of the general population.[25-28] The main causes of elevated mortality may be attributed to cardio/cerebrovascular accidents, respiratory diseases, infections, and secondary malignancies. These phenomena are speculated to be related to excessive hormone secretion (especially of growth hormone and corticotropic hormone), hypopituitarism, hormone replacement therapy, and therapeutic intervention, such as surgery and irradiation. In this study, Overall survival rates at 3 and 5years were 92%, and 83%, respectively. Overall survival of patient who received adjuvant radiation had better survival as compared to those who did not receive adjuvant radiation i.e. (84% vs 76%, p=.833), which are comparable to a

SEER database study in 2004–2016 conducted by Chen et al.[29]

The limitation of this study was a single centre study, sample size was small.

CONCLUSION

Radiotherapy is an effective treatment for pituitary adenomas, able to achieve excellent disease control. Patients with pituitary adenomas should be identified at an early stage so that effective treatment can be implemented. Initial therapy is generally transsphenoidal surgery with irradiation reserved for patients who do not achieve adequate reduction in tumor size after surgery.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Vandeva S, Jaffrain-Rea ML, Daly AF, Tichomirowa M, Zacharieva S, et al. The genetics of pituitary adenomas. Best Pract Res Clin Endocrinol Metab. 2010;24(3):461-76.
2. Molitch ME. Diagnosis and Treatment of Pituitary Adenomas: A Review. JAMA. 2017;317(5):516-24.
3. Ezzat S, Asa SL, Couldwell WT, Barr CE, Dodge WE, et al. The prevalence of pituitary adenomas: a systematic review. Cancer. 2004;101(3):613-9.
4. Agustsson TT, Baldvinsdottir T, Jonasson JG, Olafsdottir E, Steinthorsdottir V. The epidemiology of pituitary adenomas in Iceland, 1955-2012: a nationwide population-based study. Eur J Endocrinol. 2015;173(5):655-64.
5. Freda PU, Beckers AM, Katznelson L, Molitch ME, Montori VM. Endocrine Society. Pituitary incidentaloma: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(4):894-904.
6. Melmed S. Pituitary-Tumor Endocrinopathies. N Engl J Med. 2020;382(10):937-50.
7. Swearingen B. Update on pituitary surgery. J Clin Endocrinol Metab. 2012;97(4):1073-81.
8. Ammirati M, Wei L, Ciric I. Short-term outcome of endoscopic vs microscopic pituitary adenoma surgery: a systematic review and meta-analysis. J Neurol Neurosurg Psych. 2013;84(8):843-9.
9. Ciric I, Ragin A, Baumgartner C, Pierce D. Complications of transsphenoidal surgery. Neurosurg. 1997;40(2):225-36.
10. Barker FG II, Klibanski A, Swearingen B. Transsphenoidal surgery for pituitary tumors in the United States, 1996-2000.J Clin Endocrinol Metab. 2003;88(10):4709-4719.
11. Cote DJ, Alzarea A, Acosta MA, Hulou MM, Huang KT, Almutairi H, et al. Predictors and rates of delayed symptomatic hyponatremia after transsphenoidal surgery: a systemastic review. World Neurosurg. 2016;88:1-6.
12. Loeffler JS, Shih HA. Radiation therapy in the management of pituitary adenomas. J Clin Endocrinol Metab. 2011;96(7:1992-2003.
13. Ding D, Starke RM, Sheehan JP. Treatment paradigms for pituitary adenomas. J Neurooncol. 2014;117(3):445-57.
14. Gupta T, Chatterjee A. Modern radiation therapy for pituitary adenoma: review of techniques and outcomes. Neurol India. 2020;68(Suppl S1):113-2.
15. Katznelson L, Laws Jr ER, Melmed S, Molitch ME, Murad MH, Utz A, et al. Endocrine Society. Acromegaly: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2014;99(11):3933-51.
16. Nieman LK, Biller BM, Findling JW, Murad MH, Newell-Price J, Savage MO, et al. Endocrine Society. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015;100(8):2807-31.
17. Chanson P, Raverot G, Castinetti F, Cortet-Rudelli C, Galland F, Salenave S. French Endocrinology Society non-functioning pituitary adenoma work-group. Management of clinically nonfunctioning pituitary adenoma. Ann Endocrinol (Paris). 2015;76(3):239-47.
18. Melmed S, Casanueva FF, Hoffman AR, Kleinberg DL, Montori VM, Schlechte JA, et al. Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. The J Clin Endocrinol Metabol. 2011;96(2):273-88.
19. Gruppetta M, Mercieca C, Vassallo J. Prevalence and incidence of pituitary adenomas: a population based study in Malta. Pituitary. 2013;16:545-53.
20. Raappana A, Koivukangas J, Ebeling T, Pirilä T. Incidence of pituitary adenomas in Northern Finland in 1992–2007. J Clin Endocrinol Metabol. 2010;95(9):4268-75.
21. Tjörnstrand A, Gunnarsson K, Evert M, Holmberg E, Ragnarsson O, Rosén T, et al.. The incidence rate of pituitary adenomas in western Sweden for the period 2001-2011. Eur J Endocrinol. 2014;171(4):519-26.
22. Radhakrishnan K, Mokri B, Parisi JE, O'Fallon WM, Sunku J, Kurland LT. The trends in incidence of primary brain tumors in the population of Rochester, Minnesota. Ann Neurol. 1995;37(1):67-73.
23. Tardivo V, Penner F, Garbossa D, Di Perna G, Pacca P, Salvati L, et al. Surgical management of pituitary adenomas: does age matter? Pituitary. 2020;23(2):92-102.
24. Lobatto DJ, de Vries F, Zamanipoor Najafabadi AH, Pereira AM, Peul WC, Vliet Vlieland TP, et al. Preoperative risk factors for postoperative complications in endoscopic pituitary surgery: a systematic review. Pituitary. 2018;21(1):84-97.
25. Clayton RN, Raskauskiene D, Reulen RC, Jones PW. Mortality and morbidity in Cushing’s disease

over 50 years in Stokeon-Trent, UK: audit and meta-analysis of literature. J. Clin. Endocrinol. Metab. 2011;96(3):632-42.
26. Nilsson B, Gustavsson-Kadaka E, Bengtsson BA, Jonsson B. Pituitary adenomas in Sweden between 1958 and 1991: Incidence, survival, and mortality. J. Clin. Endocrinol. Metab. 2000;85(4):1420-5.
27. Ntali G, Capatina C, Fazal-Sanderson V, Byrne JV, Cudlip S, Grossman AB, et al. Mortality in patients with non-functioning pituitary adenoma is increased: systematic analysis of 546 cases with long follow-up. Eur J Endocrinol. 2016;174(2):137-45.
28. Javanmard P, Duan D, Geer EB. Mortality in patients with endogenous Cushing's syndrome. Endocrinol Metabol Clin. 2018;47(2):313-33.
29. Chen C, Hu Y, Lyu L, Yin S, Yu Y, Jiang S, et al. Incidence, demographics, and survival of patients with primary pituitary tumors: a SEER database study in 2004–2016. Sci Rep. 2021;11(1):1-9.

Cite this article as: Tali TA, Amin F, Sofi SR, Khan NA, Dar JA, Sofi MA. Clinico-epidemiological profile and treatment outcome of pituitary adenomas: a retrospective study. Int J Res Med Sci 2023;11:2181-5.