Pituitary Adenoma Prevalence and Characteristics in Sultan Qaboos University Hospital (SQUH): A Single Center Experience

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Abstract

Objective: In this longitudinal, descriptive study, we aimed to estimate the incidence of pituitary adenomas (PA) in adult patients and describe its epidemiological, clinical, and radiological characteristics.

Methods: We reviewed 112 records of all PA patients from January 2015 to January 2020 at the Endocrinology units (clinic and ward) of Sultan Qaboos University Hospital (SQUH).

Results: The incidence of PA among adults at SQUH (inpatient and outpatient) over five years (2015-2020) was 0.23%. The cohort had a mean age of 41±15. Approximately 70.5% (n=79) of the patients were women with a female: male ratio of (79/33). About 45.5% of adenomas were prolactinomas (n=51, males: n=11 (21.65%) and Females: n=40 (78.4%)), 41.1% were non-functioning adenomas (n=46), 6.2% were Growth hormone-secreting adenomas (n=7), and 5.3% (n=6) were ACTH secreting adenoma. Headache was present in 59.8% (n=67) of the patients, followed by menstrual cycle abnormalities in women (41.1%, n=46), visual field defects (35.7%, n=40), galactorrhea (23.2%, n=26), and fatigue (19.6%, n=19). The radiological appearance of adenoma was nearly equally distributed between micro- and macroadenomas. In comparison, macroadenomas constituted about 49.1% (n=55). About 52% (n=58) of the PAs were treated medically by cabergoline, octreotide and replacement therapy such as hydrocortisone and thyroxin, 34% were treated surgically (n=38), mainly by trans-sphenoidal pituitary resection), and the remaining 8.9% (n=10) were treated with radiotherapy. Medical treatment combined with surgery was employed for about 13.4% (n=15) of the patients, and radiotherapy was used for about 8.9% (n=10).

Conclusions: In our investigation, PA was primarily prevalent among female patients, and the most common subtype of pituitary tumors was prolactinomas. The majority of the patients presented with headaches and menstrual irregularities. Medical treatment was the primary approach for the applicable types of PAs, while surgery and radiotherapy were found to be secondary and tertiary treatment options, respectively.

Keywords: Pituitary adenoma; Non-functional Pituitary Adenoma; Acromegaly; Prolactinoma.

Introduction

Pituitary adenomas (PA) are the most common sellar mass lesions, accounting for 15% of all intracranial tumors.[1] A significant percentage of PAs, approximately 60-70%, secrete excess hormones. The remaining 25-35% are non-functioning (silent) tumors.[2]

The prevalence of PA has been previously investigated.[3] One of the first attempts to estimate the prevalence of PA in autopsy samples was in 1936, when it was found in 22.5% of unselected cases. This suggests that PAs can be discovered during an autopsy of individuals who did not exhibit PA symptoms.[3] Moreover, radiological studies identified PA in asymptomatic individuals at a high prevalence rate of 10–38%.[4] Furthermore, the prevalence of PA in tertiary referral centers was estimated to be around 190-280/million in the UK and about 190/million in Italy.[5]

The prevalence of PA varies by age and sex. In males, PA is more prevalent than in females over the age of 70. In contrast, in females, it is more common under the age of 50, with a peak incidence between 20 and 39 years old. For men, the prevalence of PA increases during their sixth decade of life, with a peak incidence between 50 and 60 years of age.[6]

This study aimed to assess the incidence of PA among adult inpatients and outpatients (aged >20 years old). The significance of the study lies in the fact that estimating the incidence of PA is crucial for understanding the disease burden. Additionally, it can aid in reducing PA-related morbidity and mortality rates and enhancing patient management.

Methods

Ethical approval was obtained from the Medical & Research Ethics Committee at Sultan Qaboos University, Muscat, Oman (MERC#:2158).

All patients who presented with pituitary adenomas to the clinic or ward or were referred to the Endocrinology clinic at SQUH between January 2015 and February 2020 were included in this longitudinal study. Patient data were retrieved from the SQUH database: Track care system. Patients' identification numbers were coded to maintain confidentiality. The analysis did not interfere with the patient's management. The data analyzed included demographic information (age, gender, area of residence), comprehensive clinical evaluation, hormonal levels, treatment plan, and radiological indications of the pituitary mass lesion using MRI scans conducted at SQUH or other health facilities.

Descriptive statistics were used to describe the data. The data were analyzed using the Statistical Package for Social Science (SPSS) version 23.0. Mean and standard deviations (± SD) were reported for continuous variables, whereas categorized variables were analyzed and presented as frequencies and percentages. The results were used to estimate the incidence of non-functional pituitary adenomas in patients admitted to SQUH using the number of patients with pituitary adenomas and the total number of patients with abnormal pituitary function test and had done MRI of the pituitary fossa.

Epidemiological characteristics of patients, presenting symptoms received, and mortality rates were analyzed as different variables in SPSS.

Results

Over the five-year study period (2015-2020), a total of 112 patients with PA representing a diverse mix of the Omani population, were included in this study. The overall mean age of the cohort was 41±15 years, ranging from 20 to 96 years. The majority of patients were females (n=79; 70.5%). The most common subtype of pituitary tumors in the cohort was prolactinomas (n=51; 45.5%), followed by non-functioning adenomas (n=46; 41.1%), Growth hormone (GH)-secreting adenomas (n=7; 6.2%), and ACTH-secreting pituitary adenomas (n=6; 5.3%). The overall incidence of pituitary adenomas patients was 0.23%, giving one case of pituitary adenomas per 434 patients who were admitted to the endocrine clinic with abnormal pituitary function tests.

Patients with the most common pituitary tumors differed significantly in age (Table 1). Patients with GH-secreting pituitary adenomas were older compared to those with non-functioning adenomas (54 versus 44 years respectively), prolactinomas (54 versus 38 years, respectively), and ACTH-secreting pituitary adenomas (54 versus 31 years, respectively). Furthermore, microadenomas constituted 50.9% (n=57;) of the total cases, while macroadenomas constituted 49.1% (n=55). Subjects with non-functioning adenomas and GH-secreting pituitary adenomas were more likely to have macroadenomas than those with either prolactinoma or ACTH-secreting pituitary adenomas (71.4% (n=5) and 60.9% (n=26) versus 43.1% (n=22) and 50.0% (n=3), respectively).

Table 1: Demographic and tumor characteristics of the four most prevalent pituitary tumors in the evaluated cohort.

Characteristics	NFPA (n=46)	Prolactinoma (n=51)	GH-secreting pituitary adenoma (n=7)	ACTH-secreting pituitary adenoma (n=6)	All adenomas (n=112)
Age, mean ± SD	44±17	38±9	54±24	31±12	41±15
Male gender, n (%)	18 (39.1%)	11 (21.6%)	3 (42.9%)	1 (16.7%)	33 (29.5%)
Female gender, n (%)	28 (60.9%)	40 (78.4%)	4 (57.1%)	5 (83.3%)	79 (70.5%)
Microadenoma, n (%)	18 (39.1%)	29 (56.9%)	2 (28.6%)	3 (50.0%)	57 (50.9%)
Macroadenoma, n (%)	28 (60.9%)	22 (43.1%)	5 (71.4%)	3 (50.0%)	55(49.1%)

Abbreviations: NFPA= non-functioning pituitary adenomas.

The most prevalent specific clinical manifestation of PA were headaches (n=67; 59.8%), menstrual irregularities (n=45; 57%), visual field defects (n=40; 35.7%), galactorrhoea (n=26; 23.2%) and fatigue (n=9; 19.6%) (Table 2). Menstrual irregularities were mostly associated with patients with prolactinomas and non-functioning adenomas rather than those with GH-secreting pituitary adenomas or ACTH-secreting pituitary adenomas (67.5% and 57.1% versus 25% versus 20%, respectively). Galactorrhoea was mostly associated with patients with prolactinomas rather than patients with non-functioning adenomas, acromegaly, or ACTH-secreting pituitary adenomas (41.2% versus 10.9% versus 0% versus 0%, respectively). Furthermore, hypopituitary symptoms were most associated with those with non-functioning adenomas rather than those with either prolactinomas, acromegaly, or ACTH-secreting pituitary adenomas (17.4% versus 3.4% versus 0% versus 0%, respectively). Incidentally detected PAs accounted for 5.3% (n=6) of total patients. The oldest patient diagnosed in this study was 96 years old and was incidentally found to have functional microadenomas secreting growth hormone, diagnosed as acromegaly and treated with octreotide.

Table 2: Clinical presentation of the four most prevalent pituitary tumors in the evaluated cohort.

Feature	NFPA (n=46) F=28	Prolactinoma (n=51) F=40	GH-secreting pituitary adenoma (n=7) F=4	ACTH-secreting pituitary adenoma (n=6) F=5	All adenomas (n=112) F=79
Headache, n (%)	26 (56.5%)	36 (37.6%)	3 (42.9%)	2 (33.3%)	67 (59.8%)
Fatigue, n (%)	9 (19.6%)	6 (11.8%)	2 (28.6%)	1 (16.7%)	19 (17.0%)
Visual field defects, n (%)	16 (34.8%)	20 (39.2%)	1 (14.3%)	2 (33.3%)	40 (35.7%)
Menstrual cycle abnormality in women, n (%)	16 (57.1%)	27 (67.5%)	1 (25%)	1 (20%)	45 (57%)
Galactorrhoea, n (%)	5 (10.9%)	21 (41.2%)	0 (00.0%)	0 (00.0%)	26 (23.2%)
Hypopituitary symptoms, n (%)	8 (17.4%)	4 (7.8%)	0 (00.0%)	0 (00.0%)	12 (10.7%)
Other neurological signs, n (%)	28 (60.9%)	37 (72.5%)	3 (42.9%)	2 (33.3%)	70 (62.5%)

Abbreviations: NFPA= non-functioning pituitary adenomas.

In this series we did not note any spontaneous resolution of tumors. Several therapeutic options were used for the treatment of the different pituitary tumors. These included medical treatment, surgery, medical plus surgery, and radiotherapy (Table 3). PAs were treated medically by Cabergoline and Octreotide. In addition, Hydrocortisone and Thyroxine was used as a replacement therapy. Surgery is indicated for macroadenomas with visual disturbance and

symptomatic non-functional adenomas with symptoms due to compression effects. The most common treatment options were medical treatment (n=58; 51.8%), followed by surgically (n=38; 33.9%), medical plus surgery (n=15; 13.4%), and finally, radiotherapy (n=10; 8.9%).

Table 3: Therapeutic modalities of the four most prevalent pituitary tumors in the tested cohort.

Therapeutic option	NFPA (n=46) F=28	Prolactinoma (n=51) F=40	GH-secreting pituitary adenoma (n=7) F=4	ACTH-secreting pituitary adenoma (n=6) F=5	All adenomas (n=112) F=79
Medical, n (%)	4 (8.7%)	43 (84.3%)	5 (71.4%)	3 (50.0%)	58 (51.8%)
Surgery, n (%)	20 (43.5%)	10 (19.6%)	6 (85.7%)	5 (83.3%)	38 (33.9%)
Medical + surgery, n (%)	3 (6.5%)	6 (11.8%)	4 (57.1%)	2 (33.3%)	15 (13.4%)
Radiotherapy, n (%)	7 (15.2%)	3 (5.9%)	1 (14.3%)	1 (16.7%)	10(8.9%)

Abbreviations: NFPA= non-functioning pituitary adenomas.

Patients with prolactinoma were mostly treated medically (n=43; 84.3%), and in less extent surgically (n=10; 19.6%). Surgical intervention was indicated in patients with GH-secreting pituitary adenomas (n=6; 85.7%), ACTH-secreting pituitary adenomas (n=5; 83.3%) and non-functioning adenomas (n=20; 43.5%). Some patients with non-functioning adenomas were treated by radiotherapy as a post-operative treatment to prevent recurrence (n=7; 15.2%).

Discussion

Epidemiological studies are critical for accurately quantifying disease incidence, severity, and healthcare resource utilization. This study aimed to investigate the incidence of pituitary adenomas in adult patients by analyzing hospital records of 112 patients over a five years study period. The mean age of our cohort was 41 years, which is consistent with the findings of a study conducted in Iceland (44 years).[7] However, a previous study conducted in Oman in 2007 reported a mean age of 33 years.[8]

The prevalence and occurrence of non-functioning pituitary adenomas (NFPAs) is rising in recent years, with a relative reduction in other subtypes.[9] This can be attributed to the current advances in imaging facilities, which have led to the discovery of incidentalomas, most of which are NFPAs,[8] that as typically non-secreting tumors, and are not detected till they grow and cause compression symptoms. This also may explain the higher incidence of microadenomas observed in post-mortem studies.[10] Prolactinomas predominantly presented as microadenomas with an early presentation of hormonal changes and abnormal menstrual irregularities in females.[8,11]

In our cohort, the incidence of PA was higher in females (70.5%) than in males (29.5%), which was consistent with previous studies conducted in the Middle East. In one similar study conducted in a community-based hospital in Saudi Arabia, the incidence in females was reported as 71.9%,[12] and in another recent study conducted in 2020 in the United Arab Emirates, a high incidence in female was also reported, approximately 62.5%.[13] This female predominance may be attributed to potential hormonal fluctuations throughout life.

In subtype classification, prolactinomas were the most common in our cohort (45.5%), followed by NFPA (41.1%), GH- secreting PA (6.2%), and ACTH-secreting PA (5.3%). Previous clinical prevalence studies also identified prolactinomas as the most common subtype.[13-15] Moreover, our findings contradict studies that reported a higher incidence of NFPA (43.1%) compared to prolactinoma (39.9%).[7] Additionally, another study by Faglia G (1993) reported a higher incidence of NFPA (50.6%) than prolactinoma (36.9%).[10] Moreover, the incidence of GH-secreting PA (11.2%) was almost double compared to our observation.[7] In comparison to a previous study conducted in Oman by Al- Futaisi[8] the incidence rate of NFPAs reduced from 50.6% to 43.1%.

In this study, the non-functioning PAs were predominantly macroadenomas (60.9%). Similar results were reported in a cohort from Iceland, where NF pituitary macroadenomas accounted for 74.4% of cases.[7] The likely explanation

for the higher incidence of these non-functioning pituitary macroadenomas could be their asymptomatic behavior until they enlarge and present with compression symptoms, which may also explain the higher incidence of microadenomas in post-mortem studies.[10]

On the other hand, prolactinomas were predominantly microadenomas (56.9%), possibly due to their early presentation of hormonal changes and an abnormal menstrual cycle in women. These results are consistent with the findings of previous studies (57.43%, 86%).[8,16]

In our cohort, the primary clinical manifestations were headache (59.8%), menstrual irregularities (41.1%), and visual field defects (35.7%). Studies conducted in the UK and UAE have shown that one of the most frequent presentations of the patients was a headache.[13,14] Prolactinomas were the most frequent adenomas in our patients (n=51). They were mainly associated with menstrual irregularities (52.9%) such as amenorrhea, oligomenorrhea, and galactorrhoea (41.2%), which concurs well with previously reported studies in which the most prevalent symptoms were amenorrhea-galactorrhea (84.7%) for patients with prolactinomas.[10,13] 17.4% of patients reported symptoms of hypopituitarism with non-functioning adenomas, which is also almost consistent with previous findings of 8.7%.[8]

Among the therapeutic modalities, our results showed that the most common option used was medical treatment (51.8%), followed by surgery (33.9%), medical plus surgery (13.4%), and lastly, radiotherapy (8.9%). Although in a lower percentage, similar management strategies were reported previously including medical treatment (39%), required surgery (21%), and surgery plus medical (n=3; 2%).[8] However, these results differ from studies conducted on a Swedish cohort that reported a higher rate of surgical management (55%) followed by medical therapy (45%) and radiotherapy (<1%) in comparison to our study, respectively.[17]

Our findings and the Swedish study's findings showed that a small percentage of patients received radiotherapy as a treatment modality. Radiotherapy was the standard treatment option for patients with PAs until the late 1980s when it was found to increase the chance of secondary tumor development and may result in cognitive impairment.[18]

Conclusion

In this study, PA patients were predominantly females, and its most common subtype was prolactinomas. PAs were primarily associated with headaches and menstrual irregularities. Moreover, PA patients were mainly treated medically, followed by surgery and radiotherapy to a less extent as a second and third option. This study presents up-to-date PA incidence rates at a single center, as well as a detailed overview of its various subtypes. We have affirmed recent findings and provided a detailed examination of the epidemiology of pituitary adenomas by examining a well-defined population.

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References

1. Yedinak CG, Fleseriu M. Self-perception of cognitive function among patients with active acromegaly, controlled acromegaly, and non-functional pituitary adenoma: a pilot study. Endocrine 2014 Aug;46(3):585-593.

2. Snyder PJ. Clinical manifestations and diagnosis of gonadotroph and other clinically nonfunctioning pituitary adenomas. 2014. Available at: https://ezproxysrv.squ.edu.om:2216/contents/clinical-manifestations-and-diagnosis-of- gonadotroph-and-other-clinically-nonfunctioning-pituitary-adenomas?search=pituitary adenoma&source=search_result&selectedTitle=2~150&usage_type=default&display_ra nk=2#H12 (Accessed: March 14, 2020).

3. Costello RT. Subclinical adenoma of the pituitary gland. Am J Pathol 1936 Mar;12(2):205-216.1.

4. Vasilev V, Rostomyan L, Daly AF, Potorac I, Zacharieva S, Bonneville JF, et al. MANAGEMENT OF ENDOCRINE DISEASE: Pituitary 'incidentaloma': neuroradiological assessment and differential diagnosis. Eur J Endocrinol 2016 Oct;175(4):R171-R184.

5. Clayton RN. Sporadic pituitary tumours: from epidemiology to use of databases. Baillieres Best Pract Res Clin Endocrinol Metab 1999 Oct;13(3):451-460.

6. Aflorei ED, Korbonits M. Epidemiology and etiopathogenesis of pituitary adenomas. J Neurooncol 2014 May;117(3):379-394.

7. Agustsson TT, Baldvinsdottir T, Jonasson JG, Olafsdottir E, Steinthorsdottir V, Sigurdsson G, et al. The epidemiology of pituitary adenomas in Iceland, 1955-2012: a nationwide population-based study. Eur J Endocrinol 2015 Nov;173(5):655-664.

8. Al-Futaisi A, Saif AY, Al-Zakwani I, Al-Qassabi S, Al-Riyami S, Wali Y. Clinical and epidemiological characteristics of pituitary tumours using a web-based pituitary tumour registry in Oman. Sultan Qaboos Univ Med J 2007 Apr;7(1):25-30. http://www.omands.org:2082/frontend/rvblue/files/. Accessed 21 Dec 2020.

9. Chen Y, Wang CD, Su ZP, Chen YX, Cai L, Zhuge QC, et al. Natural history of postoperative nonfunctioning pituitary adenomas: a systematic review and meta-analysis. Neuroendocrinology 2012;96(4):333-342.

10. Faglia G. Epidemiology and pathogenesis of pituitary adenomas. Acta Endocrinol (Copenh) 1993 Jul;129(Suppl 1):1-5. https://europepmc.org/article/med/8396832. Accessed 22 Apr 2021.

11. Cury ML, Fernandes JC, Machado HR, Elias LL, Moreira AC, Castro Md. Non-functioning pituitary adenomas: clinical feature, laboratorial and imaging assessment, therapeutic management and outcome. Arq Bras Endocrinol Metabol 2009 Feb;53(1):31-39.

12. Aljabri KS, Bokhari SA, Assiri FY, Alshareef MA, Khan PM. The epidemiology of pituitary adenomas in a community-based hospital: a retrospective single center study in Saudi Arabia. Ann Saudi Med 2016;36(5):341-345.

13. Aldahmani KM, Sreedharan J, Ismail MM, Philip J, Nair SC, Alfelasi M, et al. Prevalence and characteristics of sellar masses in the city of Al Ain, United Arab Emirates: 2010 to 2016. Ann Saudi Med 2020;40(2):105-112.

14. Fernandez A, Karavitaki N, Wass JA. Prevalence of pituitary adenomas: a community-based, cross-sectional study in Banbury (Oxfordshire, UK). Clin Endocrinol (Oxf) 2010 Mar;72(3):377-382.

15. Gruppetta M, Mercieca C, Vassallo J. Prevalence and incidence of pituitary adenomas: a population based study in Malta. Pituitary 2013 Dec;16(4):545-553.

16. Day PF, Loto MG, Glerean M, Picasso MF, Lovazzano S, Giunta DH. Incidence and prevalence of clinically relevant pituitary adenomas: retrospective cohort study in a Health Management Organization in Buenos Aires, Argentina. Arch Endocrinol Metab 2016;60(6):554-561.

17. 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 Oct;171(4):519-526.

18. Ecemis GC, Atmaca A, Meydan D. Radiation-associated secondary brain tumors after conventional radiotherapy and radiosurgery. Expert Rev Neurother 2013 May;13(5):557-565.