RESEARCH ARTICLE

Prioritizing Pituitary Adenoma Care in Pakistan: Analysis from an Epidemiological Study

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Abstract

Objective: To identify symptoms and risk factors and promptly diagnose, treat, and manage pituitary adenomas. Prioritizing care for pituitary adenomas will reduce the prolonged disability.

Methods: Patients with a histopathological diagnosis of a pituitary adenoma that presented at 32 tertiary care neurosurgical centres were included. The information recorded included demographics, treatment methods, adjuvant chemoradiotherapy and loss to follow-up. Data on tumour size, functionality, and laterality were collected.

Results: Of the 32 hospitals surveyed, 24 operated on pituitary adenomas, and treated 277 patients. The mean age at diagnosis was 39.8 ± 13 years, with a majority of males (63.5%) being diagnosed than females. Paediatric cases constituted only 4.7% of the total pituitary adenomas operated upon. Gross total resection was reported for 155 (56%) of all pituitary adenoma patients. Majority of the patients affected by pituitary adenomas (80.1%) were from the working class.

Conclusion: Highlighting care for non-malignant brain tumours is important for Pakistan's health system. Evidence pertaining to gender and age disparities indicates that males in the younger age groups are predominantly affected, which takes a large socio-economic toll on patients and their households. This study also highlights the need to incorporate digital health technologies for postoperative follow-up and adjuvant treatment.

Keywords: Pituitary Neoplasms, Chemoradiotherapy, Healthcare, Socioeconomic Factors, Demography.

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Introduction

Pituitary adenomas are a type of non-malignant intracranial tumours. However, tumours may become aggressive and often require multidisciplinary care.[1] Although generally a non-malignant tumour, pituitary adenomas can have debilitating complications if left untreated. Therefore, it is necessary to diagnose and treat pituitary adenomas promptly. Prioritizing care for pituitary adenomas will reduce the chances of functional disabilities and prolonged illness.

The 5-year overall survival for pituitary adenomas is 89%.[2] The post-treatment 10-year progression-free survival for pituitary adenoma patients is 94%, and the 20-year overall survival is 88%.[3] This indicates that with both surgical treatment and timely follow-up management, patients with pituitary adenomas have a favourable prognosis for both progression-free and overall survival.[4] These survival outcomes reiterate that adequate, prompt treatment can result in patients returning to their functional status prior to the onset of disease.

The incidence and prevalence of pituitary adenomas are not known in Pakistan. A study carried out at a private tertiary care facility in Karachi, Pakistan, assessed medical records from 1995 to 2005 to determine epidemiological patterns of pituitary adenomas and found that 63% of pituitary adenoma patients were male, and the mean age at diagnosis was 37 years.[5] This is significant for the Pakistani context, as it indicates a skew towards younger population and with a male bias. However, this study was conducted in a single centre, and the results cannot be extrapolated to the entire country. Furthermore, this study was carried out over a decade ago, and no epidemiological analysis of pituitary adenomas have been reported in recent years.

To address the evidence and knowledge gap in brain tumour epidemiology, The Pakistan Association of Neuro-oncology (PASNO) carried out a retrospective, cross-sectional study known as the Pakistan Brain Tumour Epidemiology Study (PBTES),[6] the results of which are being published in this supplement. From this study, we found that pituitary adenomas were the third most common type of brain tumour being surgically treated in

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Pakistan and therefore warranted a separate analysis of patient characteristics and treatment strategies. We posit that it is the responsibility of the health system to ensure safe and quality access to holistic treatment and management of non-malignant tumours such as pituitary adenomas as they are easy to treat, have a promising prognosis and, in Pakistan, affect the working-age population, leading to productivity loss, if left inadequately treated. The onus falls on both the public and private health sectors to bridge the unmet care need.

Methods

The Pakistan Brain Tumour Consortium (PBTC) was established with at least one neurosurgeon attending and one resident from each participating neurosurgical centre. The purpose of the group was to collect case data and establish a collaborative network of the neuro-oncological workforce in Pakistan. Inclusion criteria contained patients with a histopathological diagnosis of pituitary adenoma that presented at the 32 participating centres- all pituitary adenoma cases that were reportedly made up the sample for this analysis. The centres included had dedicated neurosurgical facilities. The information recorded included demographics, treatment methods, adjuvant chemoradiotherapy and loss to follow-up (LTFU), which was declared if medical records at the primary surgical care centre did not reflect follow-up at the same centre with the same surgeon. Students, residents, and faculty collated data from medical charts and electronic health records. SPSS Version 25.0 and STATA Version 16.0 were used to analyse data.

Patient characteristics, including age, gender, marital status, and occupation, were collected, along with medical and social histories. For surgical treatment, the extent of resection was reported by the surgeon, and postoperative imaging was not included. The pituitary adenoma subtypes that were collected included non-functioning microadenomas, functioning microadenomas, non-functioning macroadenomas, functioning macroadenomas and giant macroadenomas. Information about tumour laterality was collected. Adjuvant chemoradiotherapy history was also gathered.

Results

In Pakistan, the PBTES found that 277 pituitary adenomas had been operated on, making up 10.4% of the cases reported in 2019. Of the 32 hospitals surveyed, 24 hospitals operated on pituitary adenomas. The highest volume center operated on 53 pituitary adenomas. Pituitary adenomas were diagnosed in 176 male patients, upto 11% of all brain tumours diagnosed in 2019 and 99 females' patients, making up 8.7% of all diagnosed brain

Table-1: Demographic Characteristics.

Gender	Male	176
	Female	99
	Not specified	2
Occupation	Blue collar workers, labourers, daily wagers	112
	Graduates, mid-level office workers, homeowners	110
	Doctors, lawyers, engineers, big business owners, landowners	14
	Not Specified	41

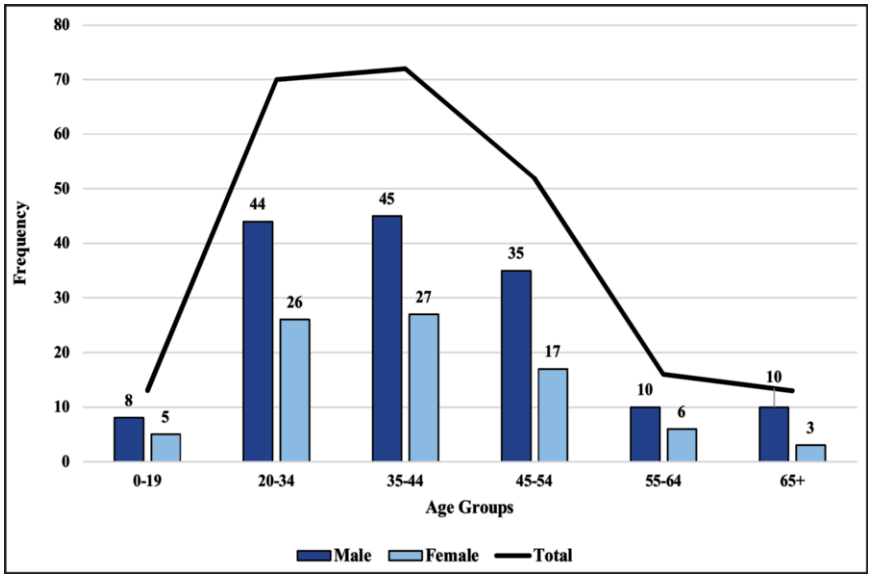

Figure-1: Pituitary Adenoma Distribution by Age and Gender.

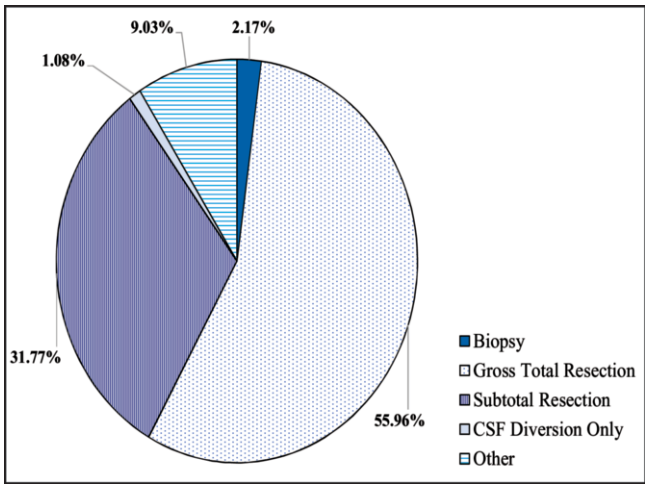

Figure-2: Extent of Resection.

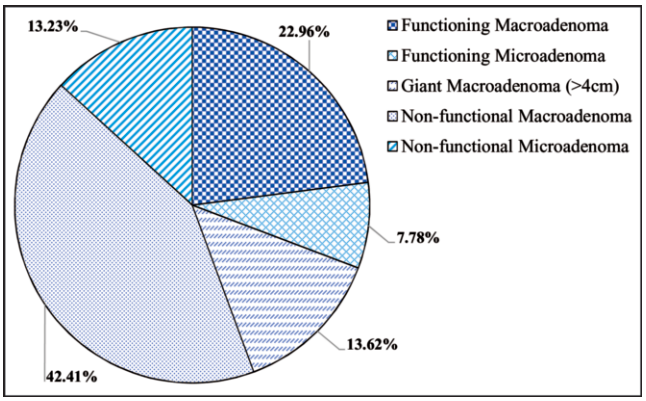

Figure-3: Pituitary Adenoma Subtypes.

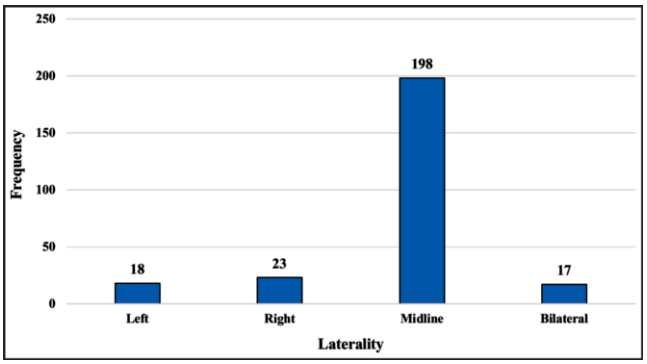

Figure-4: Pituitary Adenoma Laterality.

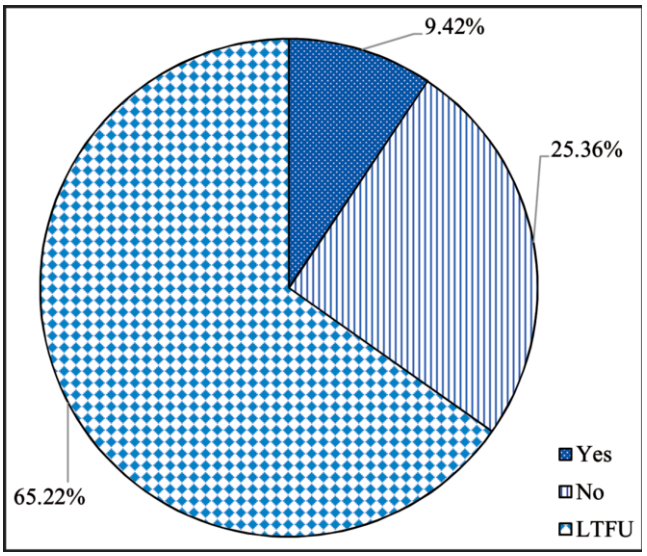

Figure-5: Radiation Therapy.

tumours. The mean age at diagnosis was 39.8 ± 13.1 years and both males and females predominantly presented between 35 and 44 years of age. Paediatric cases constituted only 4.7% of the total pituitary adenomas operated upon. No cases with other intracranial or multi-endocrine tumours were reported. Table-1 indicates that 80.1% of pituitary adenoma patients are daily wage earners, labourers, graduates, mid-level office-workers, and small homeowners. This means that patients are mainly concentrated in the low- and middle-class population.

The extent of resection for all 277 pituitary adenoma patients was noted, and gross total resection was reported for 155 (56%) of all pituitary adenoma patients. Subtotal resections frequency 88(31.8%) were the second most common type of resection. Other procedures included biopsies, cerebrospinal fluid diversions and craniotomies (not otherwise specified). Figure-2 elaborates on the surgical procedures carried out in Pakistan for pituitary adenomas.

It was found that pituitary adenomas diagnosed and operated on are largely non-functional macroadenomas 117(42.41%). Tumours were also overwhelmingly located in the midline 214(77.3%). (Figures-3 and 4)

Adjuvant radiotherapy was provided to 26(9.42%) of patients, whereas over half of the patients operated on for pituitary adenoma were LTFU. (Figure-5)

Discussion

Our study found 277 cases of pituitary adenoma reported by participating centres in 2019, of which 175(63.5%) were males. The mean age at diagnosis was 39.8 ± 13 years. Working class populations make up 80.1% of the population affected by pituitary adenomas. Gross total resection was performed on 155 (55.96%) patients, and 180 (65.22%) patients were LTFU for chemoradiotherapy.

The Socio-economic Burden of Pituitary Adenomas: Globally, pituitary adenomas disproportionately affect elderly populations over the age of 65 years.[7] In Pakistan, however, our findings show that no cases of pituitary adenoma in this age group have been reported. This may be attributed to the shorter average life expectancy in Pakistan at birth, which is 67.27 years.[8] Instead, the mean age at diagnosis in this group was 39.8 ± 13.1 years. This suggests that patients in Pakistan are being diagnosed with pituitary adenomas at younger ages. Our findings are supported by a 2008 study carried out in a private tertiary care hospital in Karachi, Pakistan, which reported the mean age of patients diagnosed with pituitary adenoma to be 37 years.[5] In Oman, which, like Pakistan, is in the Eastern-Mediterranean region, the mean age at diagnosis is 41 ± 15 years, which may indicate the earlier onset of disease in the region.[9]

Furthermore, globally pituitary adenomas also occur more commonly in females.[10] However, in Pakistan, it is

observed that males are more frequently diagnosed (63.5%). However, it is also possible that females face greater barriers to reach hospitals. Moreover, most pituitary adenoma patients are active breadwinners in their households (80.1%). Figure-1 shows a skew towards both the productive age range and a bias toward male patients. A 2018 study examining health-related productivity loss found that 41% of those surveyed reported work-related absenteeism, and 39% reported difficulty in working due to issues related to their illness. The most common complaints were mental and social concerns.[11] Extrapolating from the experiences of patients in this study, it is evident that there is a need to prioritize pituitary adenoma care in our health system. By spotlighting treatment for pituitary adenomas and offering it free at the point of care or at heavily subsidized rates, patients will be protected against financial hardship due to health and the subsequent loss of income that would otherwise be associated with disease and death.

Access to Adjuvant Treatment: Our findings indicate that 44% of the patients with surgically treated pituitary adenomas did not achieve gross total resection. However, 65.22% of patients that are operated on for pituitary adenoma are LTFU. This means that the status and outcomes of radiation therapy are not reported for these patients, and records are not kept of referrals to other hospitals for adjuvant treatment. For non-malignant tumours such as pituitary adenomas that also have a promising prognosis, the high rate of LTFU in Pakistan must be mitigated. Provisions for radiation oncology in Pakistan are, unfortunately, sparse. In the province of Punjab, an appraisal of oncological services was carried out and found that there are only 0.027 medical oncologists per 100,000 population. Each oncologist had an annual caseload of 1300 to 1500 patients, and only 21.4% of the population had access to radiation therapy.[12] Meanwhile, the recommended patient load for radiation oncologists is between 130 to 300 patients a year.[13] Data for the availability of chemoradiotherapy has not been widely reported for the rest of the country. The lack of access to oncologists and oncological infrastructure results in long wait times for care, increased costs due to long-drawn-out care, and a decrease in follow-up compliance. Unfortunately, post-surgical treatment for non-malignant tumours is often sidelined in lieu of treatment for more aggressive cancers. However, various health promotion strategies can be implemented to reduce the LTFU associated with patients diagnosed with pituitary adenomas.

Health information technologies through electronic health (eHealth) and mobile health (mHealth) can consolidate provider-patient interaction across the cancer care continuum, provide innovative and scalable opportunities for patient outreach and increase adherence to follow-up timelines.[14] In Germany, it was found that electronic patient-reported outcomes had high patient uptake usage for radiation oncology through a web app.[15] Iftikhar et al carried out an assessment of the capacity and willingness of patients with chronic conditions in Lahore, Pakistan, to use information technology and found that 90.7% of the surveyed population had cells phones, 66.2% had internet access, and half of the target population was willing to use text messages to communicate with their medical provider.[16] This is a clear indication that eHealth and mHealth provisions must be implemented to improve access to care, the number of patients covered and reduce LTFU for pituitary adenomas and other cancers alike and may be able to offset the unmet radiation therapy need. There is already set precedence in Pakistan to use mHealth technologies for childhood immunization and maternal healthcare.[17] We must learn from these experiences to expand mHealth coverage to non-communicable diseases and cancer care and pituitary adenoma management in particular. This provides further merit to the need to create centralized registries for healthcare, which will collect patient information, including contact data, that can be used to implement mHealth technologies and facilitate online care.

Conclusion

Highlighting care for non-malignant brain tumours is important for Pakistan's health system. Evidence pertaining to gender and age disparities indicates that males in younger age groups are predominantly affected, which takes a large socio-economic toll on patients and their households. The shocking loss to follow-up associated with a tumour that has such a promising prognosis emphasizes the need for consistent and innovative follow-up mechanisms to address the unmet need. Prioritizing pituitary adenoma care will ensure timely treatment and surgical and clinical outcomes for pituitary adenomas in Pakistan.

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Conflict of Interest: None to declare.

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