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Original Article

Descriptive surgical epidemiology of pituitary adenomas for a Hispanic population in Puerto Rico

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ABSTRACT

Background: Demographics and socioeconomic variables for patients with pituitary adenomas have been reported in the past. However, these studies included operated and nonoperated patients, in addition to microprolactinomas frequently diagnosed in women, revealing an elevated incidence among females. This study aimed to analyze the surgical incidence of pituitary adenomas for an adult Hispanic population in Puerto Rico over 6 years.

Methods: A retrospective and descriptive study was performed to investigate pituitary adenoma surgical incidence (per 100,000 people) among surgically treated pituitary adenomas in an adult (18 years or more) Puerto Rico Hispanic population. All new patients diagnosed with pituitary adenomas who underwent surgery at the Puerto Rico Medical Center between 2017 and 2022 were scrutinized. Inclusion criteria required a histopathological diagnosis of pituitary adenoma. Previously operated cases and non-Hispanic patients were excluded from the study. Patient characteristics were collected, along with the type of surgical treatment, tumor size, and secretory status.

Results: The analysis included 143 patients operated on for pituitary adenomas. Of these, 75 (52%) patients were male, and 68 (48%) were female. The median age of the patients was 56 years (range: 18–85). The average annual surgical incidence of adult Hispanic patients with pituitary adenomas was 0.73 surgeries/100,000 people. About 79% of the patients had non-functioning pituitary adenomas. About 94% of the patients were operated on using transsphenoidal surgery.

Conclusion: There was no sex predominance for surgical-treated pituitary adenomas in Puerto Rico. The surgical incidence for adult pituitary adenoma remained stable between 2017 and 2022.

Keywords: Demographics, Epidemiology, Ethnicity, Hispanic, Incidence, Pituitary adenoma, Race

INTRODUCTION

Pituitary adenomas are one of the most common benign brain tumors. In the US, pituitary adenomas account for 24% of primary benign intracranial neoplasms, with a 1.78 female-to-male ratio.[28] In Puerto Rico, they account for 22.8% of primary benign intracranial neoplasms.[28] The current incidence of pituitary adenomas in Puerto Rico is unknown. These tumors are usually diagnosed when they produce symptoms secondary to hormonal hypersecretion or compression of adjacent structures. However, some can be discovered during radiological workups for unrelated symptoms or after amenorrhea/infertility studies. Pituitary adenomas displaying no previous symptoms have been identified in approximately 10–14% of autopsy cases.[3,11]

In the US, only 42.3% of the patients with a pituitary adenoma diagnosis received histopathological confirmation.[28] In the last two decades, a significant increase in the incidence of pituitary adenomas has been reported in the US.[28] However, when the analysis was limited exclusively to histopathologically confirmed pituitary adenomas, a significant decrease in the incidence was observed in the last decade. Prolactinomas account for approximately 50% of new pituitary adenomas diagnosed annually, most being microprolactinomas.[9,10,24,38] Most of these microprolactinomas are identified in females.[7,10,38] Epidemiological studies reporting the incidence of pituitary adenomas do not represent the actual surgical incidence of pituitary adenomas which are operated on because they include microprolactinomas that are not operated on and do not receive histopathological confirmation. Reviewing the epidemiology of surgically treated pituitary adenomas can provide an accurate concept of the demographics of those patients undergoing surgery. To address this clinical knowledge gap, this study aimed to analyze the surgical incidence of pituitary adenoma with respect to age and sex in an adult Hispanic population of Puerto Rico.

MATERIALS AND METHODS

A retrospective and descriptive study was performed to investigate pituitary adenoma surgical incidence (per 100,000 people) with respect to age and sex among surgically treated pituitary adenomas in an adult Hispanic population admitted at the major neurosurgical center in Puerto Rico. All new patients diagnosed with a pituitary adenoma who underwent surgery at the Puerto Rico Medical Center between 2017 and 2022 were carefully scrutinized. This medical center is the highest volume center in the country with dedicated neurosurgical facilities. The study utilized the neurosurgery admission database of the University of Puerto Rico, which, for pituitary adenomas, includes the majority of all the cases operated in Puerto Rico. Inclusion criteria required a histopathological diagnosis of pituitary adenoma. Previously operated cases and non-Hispanic patients were excluded from the study. Patients with a pituitary tumor diagnosed only by radiological studies or during a hormonal workup without a histopathological diagnosis were excluded from the study. Patients younger than 18 years were excluded from the study. Patient characteristics, including age, sex, type of surgical treatment, tumor size, and tumor secretory status were collected from the neurosurgery database and the hospital's electronic health record. The tumor size was classified as microadenomas (<1 cm) or macroadenomas (1 cm or larger). Based on their hormonal secretory activity, pituitary adenomas were classified as functioning or non-functioning. The surgical incidence of pituitary adenomas per 100,000 people was calculated using the Puerto Rico population data from the US Census Bureau.[36]

RESULTS

The analysis included 143 patients operated on for pituitary adenomas. Of these, 75 (52%) patients were male, and 68 (48%) were female. The cohort's median age was 56 years (range: 18–85). The median age for females was 52 years (range: 18–78), while for males was 56 years (range: 25–85). About 94% of the patients had a macroadenoma. Eight patients presented with symptoms following an acute pituitary apoplexy event. About 79% of the patients had non-functioning pituitary adenomas. Based on their hormonal secretory activity and tumor size, 15% of the patients had a functioning macroadenoma and 6% had a functioning microadenoma. The cohort included 14 acromegalic patients (three microadenomas and 11 macroadenomas), nine patients with Cushing disease (six microadenomas and three macroadenomas), six patients with a prolactinoma (all macroadenomas), and one patient presenting acromegaly concurrently with Cushing disease (macroadenoma). The prolactinoma patients were operated on as they did not respond to medical treatment or presented with acute severe apoplexy visual symptoms. These patients were operated on as an emergency without preoperative hormonal results. About 94% of the patients were operated on using transsphenoidal surgery. Results are summarized in Table 1.

The surgical incidence per 100,000 people varied slightly throughout the study period, with the lowest in 2017 and 2020 [Table 2]. The average annual surgical incidence of adult pituitary adenomas was 0.73 surgeries/100,000 people.

DISCUSSION

Surgery is the primary treatment option for patients with symptomatic pituitary adenomas in good clinical condition.[24] However, observation is advised for incidental, asymptomatic suspected pituitary adenomas.[20,27,31] Prolactinomas are initially

Table 1: Demographics and treatment characteristics among operated patients with pituitary adenomas.

Variable	*n* (%)
Sex	
Male	75 (52)
Female	68 (48)
Tumor size	
Microadenoma	9 (6)
Macroadenoma	134 (94)
Secretory status	
Nonfunctioning	113 (79)
Functioning	30 (21)
Surgical approach	
Transsphenoidal	134 (94)
Craniotomy	9 (6)

n = number

Table 2: Surgical incidence (per 100,000 people) among operated patients with pituitary adenomas (2017–2022).

Year	Cases	Population	Incidence
2017	23	3,325,286	0.69
2018	26	3,193,354	0.81
2019	26	3,193,694	0.81
2020	17	3,285,874	0.52
2021	26	3,262,693	0.80
2022	26	3,221,789	0.81

treated with a dopamine agonist, but on some occasions, surgery is recommended.[1,6,16,23,24] Prolactinomas have a substantially higher incidence in females.[10] In the last two decades, pituitary microadenomas have been significantly more prevalent among females, while macroadenomas have been more prevalent among males.[5] The majority of these microadenomas in females are microprolactinomas.[10] The Central Brain Tumor Registry of the United States (CBTRUS) 2022 reported that for pituitary adenomas, there was a significant increase in the incidence of radiographically diagnosed pituitary tumors from 2004 to 2009 and 2009 to 2016.[28] However, for histopathologically confirmed pituitary tumors, there was a significant increase from 2004 to 2009 but a significant decrease from 2009 to 2016. This reduction observed from 2009 to 2016 in histopathologically confirmed tumors may be directly related to the increase in radiographically identified tumors, which typically do not require surgery and correlates with incidental pituitary adenomas and microprolactinomas. The National Program of Cancer Registries of the Centers for Disease Control and Prevention, the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute, and the North American Association of Central Cancer Registries report malignant tumors in all anatomical sites together with non-malignant brain and central nervous system tumors. Although the data from these registries can be utilized to investigate and report the incidence of benign pituitary adenomas, the analysis will contain non-operated and operated cases and will not document the surgical incidence of the disease.

Pituitary adenoma epidemiologic studies that include patients with nonoperated prolactinomas and radiologically diagnosed tumors without histopathological confirmation do not reveal the incidence of adenomas treated with surgery. Epidemiological studies reporting the surgical incidence of particular neurosurgical diseases have been previously documented.[18,19,21,32,34] However, no epidemiological study has reported the surgical incidence of pituitary adenomas. These specific studies evaluate a condition's surgical incidence and clinical outcomes. Understanding the surgical epidemiology of pituitary adenomas for preoperative counseling is important. This investigation attempted to calculate the surgical incidence of pituitary adenomas for a Hispanic population in Puerto Rico, comparing it to the overall pituitary adenoma incidence previously reported in the US and other countries. Puerto Rico is a US territory where 98.9% of the population identifies as Hispanic.[36] Therefore, tumor incidence rates are unlikely to be influenced by cases identified among non-Hispanics living in Puerto Rico.

Incidence according to sex

The most recent report from the CBTRUS documented that the pituitary adenoma incidence in the US/100,000 people was 4.62 overall (operated and nonoperated cases), being significantly higher for females (5.23) than for males (4.09) with a 1.78 female-to-male ratio.[28] However, the incidence among males and females was not documented for histologically confirmed pituitary adenomas. In Malta, during 2000–2011, the incidence of pituitary adenomas was significantly higher among females (6.58) relative to males (2.08), with the difference attributed by the authors to a greater disposition to microadenomas in females, despite a similar frequency for macroadenomas among either sex.[14] Similarly, data from Finland during 1992–2007 demonstrated that pituitary adenomas had a significantly higher incidence among females (5.86) than males (2.22).[29] A study from Pakistan showed that in 2019, pituitary adenomas had a 1.78 male-to-female ratio.[32,33] The authors attributed the male predominance to gender disparities in their country, as females faced significant medical attention barriers.[32] Epidemiological studies have demonstrated that in the US, pituitary adenoma incidence rates are higher in females in early life until about 50 years and then become higher in males.[13,22] This difference has been attributed to microprolactinomas occurring more frequently and at earlier ages in women than men.[7,9,13,17] In addition, microprolactinomas in females are diagnosed earlier in life as they produce disruption in the menstrual period secondary to hyperprolactinemia.[7,9,13,22] Using data from the National (Nationwide) Inpatient Sample (NIS) of the Health-care Cost and Utilization Project for hospital inpatient stays from 1997 to 2016 in the US, Ghaffari-Rafi *et al.* showed that the annual pituitary adenoma incidence was 2.80/100,000 people, exhibiting no sex difference.[12] In this study, the similar sex incidence is potentially attributed to the sole inclusion of admitted patients in contrast to epidemiological studies that include outpatients. Admitted patients will likely have more severe symptoms and undergo surgery, contrary to outpatients who are often not operated on as they are usually evaluated after incidental radiologically discovered pituitary region tumors or for medical management of prolactinomas. Using the NIS database from 2008 to 2011, Villwock *et al.* showed that the sex distribution for admissions for resection of pituitary adenomas was nearly equal.[37] A study evaluating the impact of frailty in patients who had undergone transsphenoidal pituitary adenoma surgery using the NIS

database from 2000 to 2014 documented no differences in sex distribution.[2] A recent analysis evaluating patients with surgically resected nonfunctioning pituitary adenoma at a single center over 20 years reported no sex predominance.[8] In these last three studies, the similar sex distribution can be attributed to the exclusive inclusion of operated patients compared to studies that include nonoperated patients.

Incidence according to age

The highest incidence of pituitary adenomas in the US occurs in the 65+ age group.[13,28] However, the median age at diagnosis is 51 years.[28] In Pakistan, the mean age at diagnosis is 39.8 years, with the highest incidence in the 35–44 years group, which the authors blamed on their country's shorter average life expectancy.[32] A pituitary adenoma epidemiologic study from Buenos Aires showed an overall mean age at diagnosis of 46.4 years; however, for prolactinomas, the mean age was 37.5 years, while for nonfunctioning adenomas, it was 68.7 years.[10] In this study from Puerto Rico, which included only surgical-treated pituitary adenoma patients, the population's median age was 56 years. Females presented at a younger median age than males (52 vs. 56 years).

Incidence according to ethnicity

Hispanic ethnicity in the US exhibits a higher incidence (4.51 vs. 3.82) of benign pituitary adenomas than non-Hispanics.[28] Mukherjee *et al.* showed that Hispanics have significantly fewer odds of being admitted to high-volume centers for pituitary tumor resection than US whites.[25] Despite this racial disparity, pituitary adenomas still have a higher incidence among Hispanics.

Incidence in Puerto Rico

The Puerto Rico Central Cancer Registry has collected information on cancer cases since 1950 and regularly submits the information to the CBTRUS and other cancer registries.[35] The 2015–2019 Cancer in North America (CiNA) monograph report indicated that in Puerto Rico, the percentage of tumors with histopathological confirmation for malignant brain and other central nervous system tumors was 79.8%, while for nonmalignant tumors was 64.2%.[4] However, the specific percentage for histopathological confirmed pituitary adenomas was not reported. In Puerto Rico, malignant brain and other central nervous system tumors had an incidence of 4.9/100,000 people for males and 3.4/100,000 for females.[4] However, for nonmalignant tumors, the incidence for males is 3.5/100,000 people, while for females, it is 5.6/100,000. This higher incidence of nonmalignant tumors in females reflects the higher propensity for meningiomas and microprolactinomas in females. The present study showed no sex predominance for surgical-treated pituitary adenomas in the adult Hispanic population. A previous study containing data from 2002 to 2006 showed that the estimated average surgical incidence of pituitary adenomas in Puerto Rico was 0.9 surgeries/100,000 people/year.[26] The results of the present study underestimate the true surgical incidence of pituitary adenomas operated in Puerto Rico as pediatric cases were not considered, and some adult cases operated at minor hospitals were not included. The present study revealed a lower incidence in 2017 and 2020 than in the other analyzed years. Two crucial environmental disasters could be blamed for this finding which could have significantly impacted that year's surgical incidence. At the end of 2017, Hurricane Maria severely affected Puerto Rico, which caused a significant limitation in medical access and substantial population emigration.[15,30] Similarly, in 2020, access to medical services was reduced due to the COVID-19 pandemic.

Limitations

The main limitation of this study is that it presents a retrospective data analysis with potential selection bias. All the patients in this study underwent surgical resection and were, therefore, subject to surgical selection bias. Each treating neurosurgeon decided which patient should be managed surgically and chose the surgical approach independently. Moreover, some potential surgical cases may have been observed or treated only with radiotherapy if the patient was elderly, had significant comorbidities, or declined surgery. Furthermore, the study analyzed 6 years, limiting the findings' generalizability to prior and subsequent years. The cohort did not include the entire Hispanic population of Puerto Rico; however, the information was obtained from the largest medical center, which covers approximately 90% of the country's population for neurosurgical conditions. The data collected in this study did not include postoperative surgical results; therefore, surgical and clinical outcomes could not be analyzed. Finally, this study reports the surgical incidence for a Hispanic population which may not be applied to other ethnic groups.

CONCLUSION

This study showed no sex predominance for surgical-treated pituitary adenomas in Hispanic patients in Puerto Rico. Most patients were managed using transsphenoidal surgery. About 79% of the patients had nonfunctioning pituitary adenomas. The surgical incidence for adult pituitary adenoma remained reasonably stable between 2017 and 2022. The average annual surgical incidence of surgical-treated pituitary adenomas was 0.73 surgeries/100,000 people, with a peak incidence of 0.81 surgeries/100,000 people. Future multicenter research is necessary to increase knowledge of the surgical incidence in patients undergoing pituitary adenoma surgery.

Declaration of patient consent

Patients' consent not required as patients' identities were not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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