RESEARCH ARTICLE

Schwannoma: A surgical epidemiology

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Abstract

Objective: To identify the surgical incidence and prevalence of schwannoma in our region and quantify the demographic, surgical, neoplastic, and outcome characteristics of the patients diagnosed with schwannoma.

Methods: A retrospective cross-sectional study was conducted from January 1 to December 31, 2019. Enrolled were 32 of the highest volume neurosurgical centres in Pakistan. Patients with a histopathological diagnosis of schwannoma and radiological imaging were included in the study. Medical records were reviewed for data, and SPSS version 25 was used for statistical analysis. Patients were followed up for one year, which was the duration of the study.

Results: From 2750 patients diagnosed with brain tumours, 148 patients had schwannomas. Out of these, 84 (56.8%) patients were male, and 64 (43.2%) patients were female. The mean age of the patients was 39 ± 14 years. The socioeconomic statuses of the enrolled patients were lower in 72 (53.3%) patients, middle in 57 (42.2%) patients, and upper middle to upper in 6 (4.4%) patients. All patients underwent surgery, 14 patients received radiotherapy, and two patients received chemotherapy. In our cohort, 115 (77.7%) patients presented to public sector hospitals, with only 33 (22.3%) patients presenting to private hospitals. At the end of the study period, 60 (40.5%) patients had been lost to follow-up. Of the remaining 88 patients, 75 (85.2%) were alive. The mortality rate on a one-year follow-up was 14.8%.

Conclusion: Schwannoma comprises a larger percentage of the brain tumours in our regions than reported in the literature. The high mortality rate is of particular concern and warrants further investigation to improve patient care and outcomes.

Keywords: Schwannoma, Brain neoplasm, Retrospective study, Epidemiology, LMIC

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Introduction

Schwannoma (also known as neurilemmomas) are benign tumours originating from cranial or peripheral nerves with Schwann cells. About 60% of all schwannomas are vestibular schwannoma which have an incidence rate of 1.51 per 100,000.[1] These tumours are usually sporadic and solitary. The most common type of intracranial schwannoma is the vestibular schwannoma (VS) that develops on the eighth cranial nerve and can even have a genetic disposition, particularly in patients with neurofibromatosis type 2.[2]

Acoustic neuromas (also known as vestibular schwannoma) often present with symptoms of unilateral audio vestibular impairments, sensorineural deafness, and tinnitus with or without imbalance. If these tumours remain undiagnosed, they grow in the direction of least resistance and may cause neurological symptoms due to brainstem compression and mass effect within the skull. At the turn of the 20th century, schwannomas carried a poor prognosis, with some studies reporting perioperative mortality of up to 84% and a high rate of neurological deficits in survivors.[2] Towards the mid-20th century, most acoustic neuromas were not operated on unless the tumour was large, with the result that most patients were told to wait and observe till the tumour got big enough to operate on. However, as medical technology and surgical techniques developed, diagnosis and approach got significantly better and perioperative mortality is now at 1% or less in most high-income countries (HIC).[1]

The most common age for schwannoma is between 50 to 60 years.[3] Gender and ethnicity have not been significant factors for the incidence or growth rate of schwannoma in literature.[3-5] While they are generally sporadic, schwannomas can be linked to Neurofibromatosis (NF) type 2, Carney complex and schwannomatosis. The index

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of suspicion should be high in patients with multiple tumours, as NF type 2 accounts for 3% of all schwannomas. Recently studies have started addressing molecular aspects of schwannomas, and new therapies are being considered for treatment.[6,7]

Literature mostly addresses vestibular schwannomas, as they are the most common type of schwannoma.[8] Other intracranial schwannomas are mostly addressed in case reports, and the average number in literature is quite low. According to The Central Brain Tumour Registry of the United States (CBTRUS), the most common location for vestibular schwannoma is the vestibulocochlear nerve (62.5%), followed by the remaining cranial nerves (15.6%) and the spinal cord (15.4%).[9,10] Trigeminal schwannomas make up less than 0.2% of all intracranial tumours compared to vestibular schwannomas, which make up 8-10%.[3,11]

Methods

We conducted a retrospective cross-sectional descriptive study that included patients admitted at a major neurosurgical centre (from participating centres) between January 1 and December 31, 2019. Patients with a histopathological diagnosis of schwannoma were included with no other restriction on inclusion. The centres included were the highest volume centres in the country and had dedicated neurosurgical facilities. A total of 32 centres participated in the study and reported the data on a standardised proforma.

Time to surgery was defined as the time in days between the radiological diagnosis and the date of surgery. Hospitals with an annual volume of more than 100 brain tumour cases per year were designated as high-volume centres, and those with 100 or lower cases per year were designated as low-volume centres.

The papers on methodology[12] and general findings[13] in this special supplement provide greater detail about the study process, parameters used, organization details, and the Pakistan Brain Tumour Consortium (PBTC) which made this effort possible. Socioeconomic Status (SES) used in this paper has been derived from employment status and the job type that the patients presented within their demographical history. The jobs were used to estimate socioeconomic brackets according to the classification by the Pakistan Bureau of Statistics supplement.[14] The lower socioeconomic class were blue-collar workers, labourers, daily wagers, etc. The Middle socioeconomic class were graduates, mid-level office workers, and homeowners. The upper and upper-middle socioeconomic classes were landowners and business owners.

Statistical analysis was performed using Statistical Product and Service Solutions (SPSS) version 25 and STATA version 16. The data were tested for normal distribution using the Shapiro-Wilk test. Mean, and standard deviation were reported for normally distributed data, while median with interquartile range were reported for non-normally distributed data. Percentages with total numbers were reported for all categories.

Results

Of 2750 brain tumour patients, 148 (5.4%) patients were diagnosed with schwannoma, of which 146 (98.7%) were vestibular schwannoma, one (0.65%) was trigeminal schwannoma, and one (0.65%) was glossopharyngeal schwannoma. The mean age of patients with schwannoma was 39 ± 14 years. Of our patients, 84 (56.7%) were male, and 64 (43.3%) were female. We had 72 (53.3%) patients from the lower socioeconomic class,

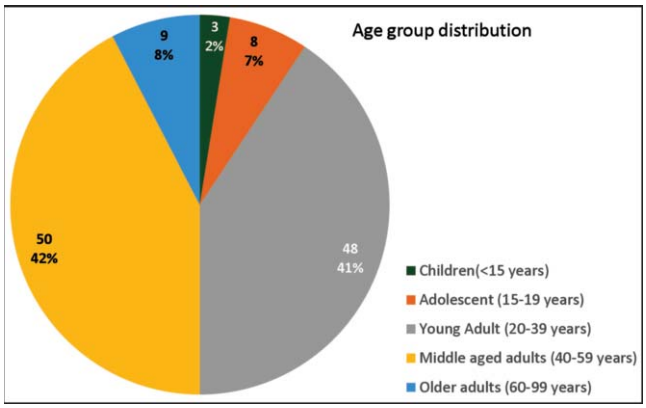

Figure-1: Distribution of age group amongst patients.

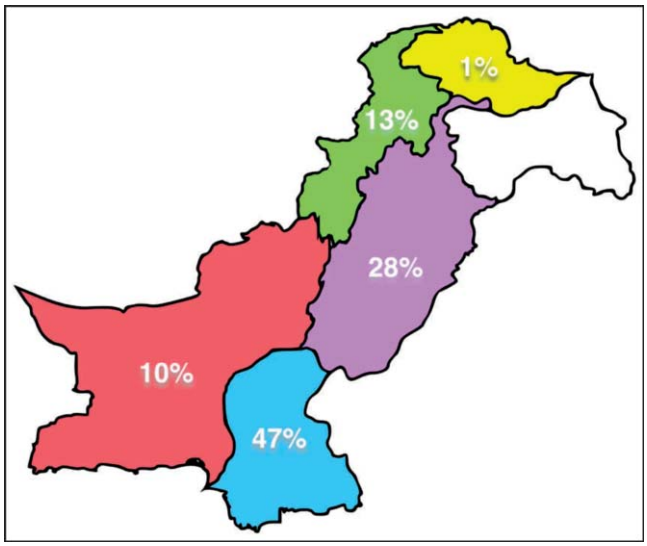

Figure-2: Provincial distribution of schwannomas.

Table-1: Demographic characteristics of patients diagnosed with schwannoma.

Demographic characteristics		n	Percentage (within group)
Age at diagnosis (mean ± SD)		39 ± 14	
Gender	Male	84	56.7%
	Female	64	43.3%
Time to surgery in days (median ± IQR)		19.5 (4 - 64.7)	
KPS score before surgery (mean ± SD)		76.5 ± 13.0	
KPS score after surgery (mean ± SD)		81.23 ± 14.3	
Socioeconomic status of patient	Lower class	72	53.3%
	Middle class	57	42.2%
	Upper middle or upper class	6	4.4%
Marital status of patient	Unmarried	20	14.6%
	Married	112	82.5%
	Other	4	2.9%
Public or private hospital	Public	115	77.7%
	Private	33	22.3%
Hospital annual patient volume	High	64	43.2%
	Low	84	56.8%
Schwannoma volume per hospital (mean)		4.6	
Current status	Alive	75	85.2%*
	Deceased	13	14.8%*
	Lost to follow up	60	40.5%**
Mortality rate	≤30 days	4.5%	
	>30 days	10.2%	

*Percentage from patients with known follow-up (n= 88)
**percentage from all patients with the tumour
SD = standard deviation
All values are from patients with known information.

57 (42.2%) patients from the middle socioeconomic class, and 6(4.4%) patients from the upper middle or upper socioeconomic class. Of our patients, 112 (82.5%) were married, 20 (14.6%) patients were unmarried, and 4 (2.9%) patients were either divorced or widowed.

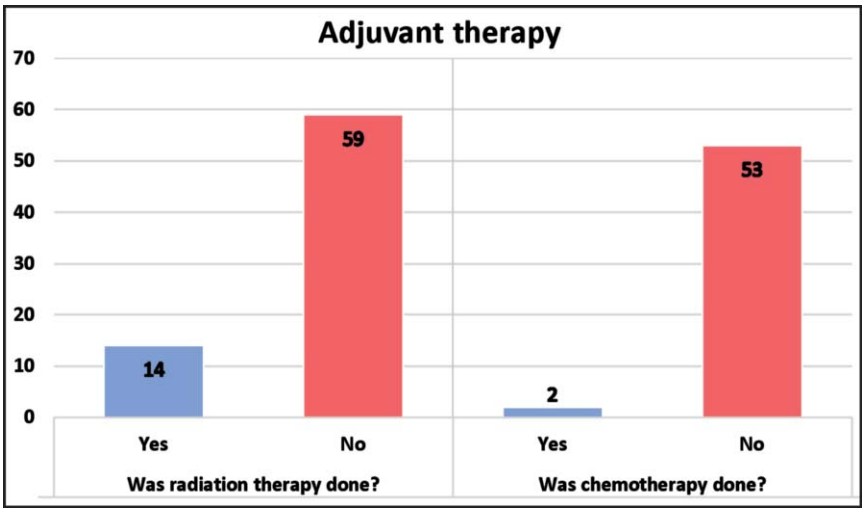

Figure-3: Adjuvant therapy received by patients (groups lost to follow-up not included).

Table-2: Provincial distribution of schwannoma cases.

Province	Population	Patients reported	Surgical incidence per 100,000
Punjab	109,989,655	37	0.03
Sindh	47,854,510	22	0.05
Khyber Pakhtunkhwa	35501964	10	0.03
Balochistan	12335129	8	0.06
Azad Kashmir	4045366	0	0.00
Gilgit Baltistan	1249000	1	0.08

All our patients underwent surgical removal of the tumour and the median time to surgery from diagnosis to surgery was 19.5 days (IQR= 4.0-64.7). The mean KPS score before surgery was 76.5 ± 13.0, and after surgery was 81.23 ± 14.3. Of our patients, 115 (77.7%) presented to public sector hospitals, with only 33 (22.3%) patients presenting to private hospitals. In our cohort, 84 (56.8%) patients presented to high-volume hospitals, with 64 (43.2%) presenting to low-volume hospitals. At the end of the study period (1 year), 60 (40.5%) patients had been LTFU, and from the remaining 88 patients, 75 (85.2%) patients were confirmed to be alive, 13 (14.8%) patients had expired. The 30-day mortality rate was 4.5%, and the overall mortality rate was 14.8%. The demographics of our patients are summarized in Table-1.

There were 3 (2%) patients aged less than 15 years old, 8 (7%) patients between the age of 15 to 18 years, 48 (41%) patients from the age of 20 to 39 years, 50 (42%) patients aged 40 to 59 years, and 9 (8%) patients aged 60 to 99 years. Our patients were mostly between the age of 20 and 59. These findings are illustrated in Figure-1.

Sindh had the highest number of patients with 37 (47%) cases, followed by Punjab with 22(28%) cases, Khyber Pakhtunkhwa at 10 (13%), Balochistan at 8 (10%) and Gilgit-Baltistan at 1(1%) case. The distribution according to province and characteristics is summarized in Table-2.

From the vestibular schwannomas, 3(0.03%) tumours were bilateral, 38(39.2%) tumours were left-sided, and 56 (57.7%) were right-sided. Of the 148 patients who underwent surgical resection, 14(9.5%) patients received radiotherapy, 59(39.9%) patients did not receive radiotherapy, and 75 (50.7%) patients were lost to follow-up. Of the 14 patients that received radiotherapy, six were those who had received gross total resection, seven had a subtotal resection,

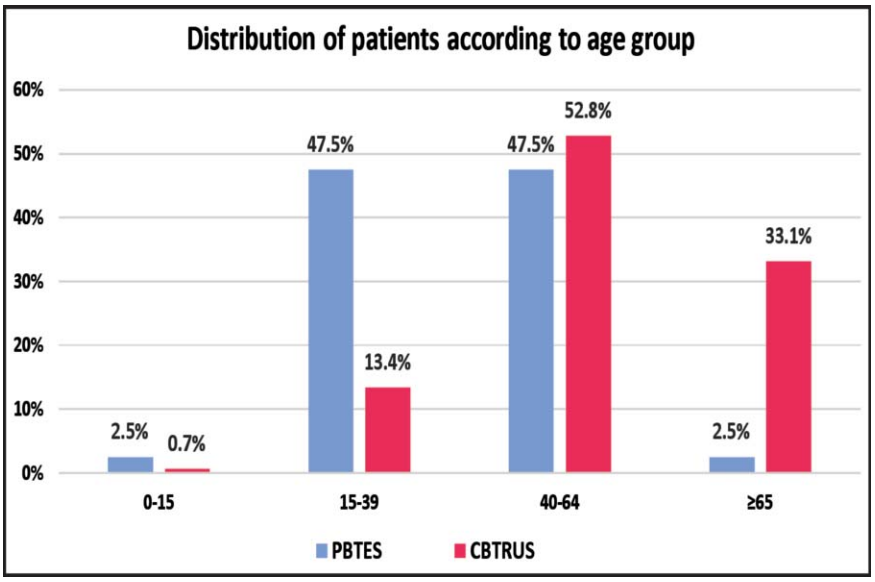

Figure-4: Patients in each age group in the PBTES and CBTRUS studies.

and 1 had unspecified surgery. Only 2 (1.4%) of our patients received chemotherapy, with 53 (35.8%) patients not receiving chemotherapy and 93 (62.8%) patients lost to follow-up. These findings are illustrated in Figure-2.

Discussion

From the total of 2750 patients with brain tumours, presenting in Pakistan in 2019 (at the included centres), 5.38% were schwannomas. While true population incidence could not be calculated due to only neurosurgical centres participating in the study, our observed ratio of schwannomas among brain tumours was higher than the rest of the world.[2,9] The most common nerve sheath tumour in the US from 2014 to 2018 was vestibular schwannoma, with an incidence of 1.2 per 100,000[9] that represented 75% of all non-malignant nerve sheath tumours, but a very small portion of overall primary brain tumours. No change in the incidence of histologically confirmed cases was observed from 2004 to 2018 in the United States. However, radiologically confirmed cases showed an increase in incidence from 2004 to 2015, followed by a significant decrease from 2015 to 2018.[9,10] The incidence of vestibular schwannoma is often quoted in literature to be one per 100,000 people.[1,11] However, a systematic review in 2021 by Marinelli et al. investigated the incidence rate of sporadic vestibular schwannoma over a period of 10 years, and the true incidence was much higher (3-5.2 per 100,000).[15]

The ratio of males to females in our population was 1.3:1, which is different from the gender ratio reported in the literature. The ratio of male to female patients was 0.89:1 in the United States over the past eight years, according to the CBTRUS report in 2021[10] which, when contrasted with our results, shows that either females remain undiagnosed in our population or there is a true difference in gender distribution of schwannoma occurrence.

Our cohort had 2.5% of patients within the 0-15 year age group compared to CBTRUS, which only had 0.7%. Likewise, we had a greater percentage of patients (47.5%) in the 15-39 year age group compared to CBTRUS (13.4%). CBTRUS had a slightly larger proportion in the 40-64 year age range compared to our population (52.8% and 47.5%, respectively). Finally, 33.1% of CBTRUS patients were greater than 65 years of age, while only 2.5% of our patients were in that age range. This comparison may be due to a true disparity in brain tumour incidence, or a more likely explanation may be the different age distribution in the population of the two countries (as with most LMICs and HICs) and lower lifespan in our region compared to the USA.[16] This comparison of distribution in our age groups and CBTRUS is illustrated in Figure-3. The most recent incidence rates for all ages in Marinelli et al.'s study were between three and 5.2 per 100,000 person-years, with the highest incident rate in patients aged above 70 (20.6 per 100,000 patient-years).[15] In our study, older age groups between the ages of 60 to 99 only comprised 8% or nine patients. This may be due to the shorter average lifespan and decreased access to health care available to older patients in our population who are often reliant on younger family members. Interestingly most cases of schwannoma in our population were in married patients, which may be representative of the age group (40-59) in which this tumour is most frequent.

The mainstay of schwannoma management is observation, surgery, radiosurgery/radiotherapy, and for patients with NF2 and rapidly growing tumours, targeted therapy with bevacizumab. Our population with schwannomas all received surgery. There is an increasing number of studies on the effects of gamma knife radiosurgery on non-vestibular schwannomas.[11] However, due to the lack of heterogeneous data and low case volume, it is difficult to suggest definitive treatment strategies applicable to most of our patients. While mortality and morbidity has improved greatly with these tumours, significant improvements could still be made,

particularly with regards to nerve preservation.

Our study comprised all patients that underwent surgical removal of schwannoma at the centres included, with 12.5% of patients receiving chemo and/or radiotherapy post-surgery (from those who were not lost to follow-up). These cases of patients receiving chemotherapy is particularly concerning as chemotherapy is not recommended for patients with a diagnosis of schwannoma unless the patient has NF2 (which we were unable to verify in our population). Radiotherapy post-surgery is only given to those who are at risk of a permanent neurological defect with complete tumour resection and thus receive only a sub-total resection.[17] In our study, two patients who underwent gross total resection subsequently underwent radiotherapy, which is a deviation from standard practice. This may signify either deviation from protocol or improper reporting of the extent of resection. Either practice is concerning and warrants further investigation at a national level. A national brain tumour registry with treatment data would be useful in recording and correcting any deviations from standardized care.

The mortality rate from patients with known outcomes at the end of the study period was 14.8% in our study, and the 30 days mortality rate was 4.5% (same as the average mortality rate for all brain tumours in our cohort). Compared with the mortality from other countries, which have rates below 1%[5] our region has a much higher mortality rate, which may be due to the late presentation, resource constraints, or lack of specialized training. As around 40.5% of our patients did not follow up, no outcome data could be obtained for those patients.

There is not much literature on the geographical distribution of schwannomas worldwide. In our region, most cases (47%) of schwannoma were from Sindh, 28% were from Punjab, 13% were from Khyber Pakhtunkhwa, and 10% were from Balochistan, and 1% were from Gilgit-Baltistan. Table-3 shows the incidence per 100,000 for the provinces (calculated according to the 2017 population census).

Punjab is the most populous province and generally has higher primary brain tumour load than the rest of the provinces at first glance; however, the incidence per 100,000 shows that it has similar hospital-based incidence as KPK. Gilgit Baltistan had the highest apparent relative incidence per 100,000 followed by Balochistan, but due to low case numbers from these provinces, an inference cannot be derived. Most of our patients seemed to prefer public sector hospitals rather than private sector hospitals 77.7% of patients presenting to government hospitals. A limitation of our study was the retrospective method with non-consecutive sampling. This was done to get a fair estimate of yearly volume. Any specific sample size calculation formula was not used.

Conclusion

Schwannoma makes up a small but significant proportion of all primary brain tumours in our region. Our experience shows that schwannoma in our region favours patients between the age of 20 and 59 years and has a much higher mortality rate than reported in high-income countries. The high mortality is especially concerning and needs further investigation to improve care.

Disclaimer: None to declare.

Conflict of Interest: None to declare.

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