

Comprehensive Analysis of Craniopharyngioma: Epidemiology, Clinical Characteristics, Management Strategies, and Role of Radiotherapy

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Abstract. *Background/Aim:* Craniopharyngiomas pose challenges in diagnosis and management due to their rare occurrence and diverse clinical manifestations. This study aimed to provide a comprehensive analysis of craniopharyngioma, including its epidemiological trends, clinical presentations, radiological characteristics, surgical interventions, and the role of radiotherapy. *Patients and Methods:* A retrospective observational study was conducted on 23 patients diagnosed with craniopharyngioma at our hospital from August 2017 to July 2019. Data regarding demographics, clinical presentation, radiological findings, surgical interventions, and adjuvant therapies were collected and analyzed. *Results:* Craniopharyngiomas exhibited a bimodal age distribution, with peaks in childhood and late adulthood. Clinical presentations varied between pediatric and adult patients, with headache and nausea/vomiting predominant in children, and visual disturbances and hypogonadism more

common in adults. Radiological imaging revealed predominantly suprasellar localization and varying tumor consistency. Surgical resection was the primary treatment modality, with post-operative complications including diabetes insipidus and cerebrospinal fluid leak. Histological analysis showed distinct subtypes, with the adamantinomatous subtype predominant in children and the papillary subtype in adults. Adjuvant radiotherapy was administered in cases of incomplete resection or tumor recurrence. *Conclusion:* This study provides comprehensive insights into the epidemiology, clinical characteristics, radiological features, surgical interventions, and role of radiotherapy in craniopharyngioma management. Understanding these aspects is crucial for tailoring optimal treatment strategies and improving patient outcomes in this complex clinical scenario.

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Key Words: Craniopharyngioma, epidemiology, clinical presentation, radiological characteristics, surgical management, radiotherapy, histological subtypes.

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The term craniopharyngioma was coined by Cushing in 1932 (1). Over the years, the tumor has been described by various other names, including tumor of Rathke's pouch, adamantinoma, ameloblastoma, craniopharyngeal duct tumor, and suprasellar cyst (1). Craniopharyngiomas are rare benign tumors of the central nervous system (CNS) with an overall incidence of 0.19 cases per 100,000 (2). They represent 1.1% of non-malignant brain and other CNS tumors (2) but are the most frequent intracranial non-glial tumors in children (3). The disease has been found to be distributed among both sexes (2, 4, 5). The tumor has peak incidence rates in children aged 5 to 14 years and adults aged 50 to 74 years (4) with a bimodal distribution. However, they may be detected at any age, with cases reported in neonates (6) and even in the prenatal period (7). They are epithelial tumors that arise from the remains of the craniopharyngeal duct.

Craniopharyngiomas may be found anywhere along the craniopharyngeal canal, but most of them arise in the sellar/parasellar region (8-10). Most of them (94-95%) have a suprasellar component whereas the purely intrasellar ones represent the least frequent variety (5-6%) (9). The predominant location of these tumors in the sellar/parasellar region and their proximity to vital structures of the brain (Figure 1) (visual pathways, hypothalamic-pituitary system, ventricular system) result in multiple clinical manifestations, which typically present as three clinical syndromes: visual disturbance, disturbance of the hypothalamic-pituitary axis, and raised intracranial pressure (11-15). The most frequently reported symptoms include headaches, nausea/vomiting, visual disturbances, failure to thrive (in children), and hypothalamic-pituitary dysfunction (in adults) (11, 13, 16). Computed tomography (CT) and magnetic resonance imaging (MRI) (Figure 2 and Figure 3) are important diagnostic tools for characterization of these tumors. Plain radiography of the skull is useful to obtain information about the size and shape of the sella and may also detect lesion calcification (17). The size of the lesion as well as its relationship to important adjacent structures, such as the pituitary gland, optic apparatus, third ventricle, and major intracranial vessels can be detected by CT and MRI (18). CT scan detects calcifications precisely in craniopharyngioma tissue, which is a finding in approximately 90% of these tumors. Contrast MRI is used to ascertain the topography and structural composition of these tumors (19). Multimodal treatment options include observation, surgical resection (subtotal or gross), irradiation, and intra-cavitary treatment [intra-cavitary irradiation or chemotherapy with Bleomycin (20) or Interferon alfa (21)]. The risk for local recurrence (22, 23) is significant and may infrequently recur at a distant site (24, 25). Recurrence may be diagnosed by routine imaging or by the recurrence of symptoms. Tumor recurrence may be treated with radiotherapy or re-operation followed by radiotherapy (26). The aim of this study was to assess the clinical and radiological features of craniopharyngioma patients across different age groups, both children and adults, and to determine their subsequent management based on morphology.

Patients and Methods

This study was a retrospective observational study conducted on patients diagnosed with craniopharyngioma at our hospital from August 2017 to July 2019. All patients with craniopharyngiomas up to 72 years of age were included in the study. Exclusion criteria comprised severely ill, obtunded children, and refusal for surgery. Each patient underwent a comprehensive assessment, including a detailed medical history, a thorough physical examination, and all pertinent investigations. Patients were followed up for a maximum of six months after discharge from the hospital. Medical records of all patients with a radiological or histological diagnosis of



Figure 1. Cerebral computed tomography angiography illustrating a sellar/suprasellar lesion encasing major blood vessels. The white arrowhead indicates the terminal part of the right internal carotid artery, partly encased by the tumor causing mild luminal narrowing. The white arrow highlights the mild luminal narrowing of the origin of the right middle cerebral artery due to encasement by the tumor.

craniopharyngioma from January 2014 to July 2017 were retrospectively retrieved from the Medical Records Department at SKIMS Srinagar. Data were recorded as available in the medical records, without adherence to a preset questionnaire or case record sheet. All data were tabulated in a Microsoft Excel spreadsheet and assessed with regard to age at presentation, sex, clinical presentation



Figure 2. FLAIR image in axial section showing a well-defined cystic space-occupying a lesion in the sellar region.

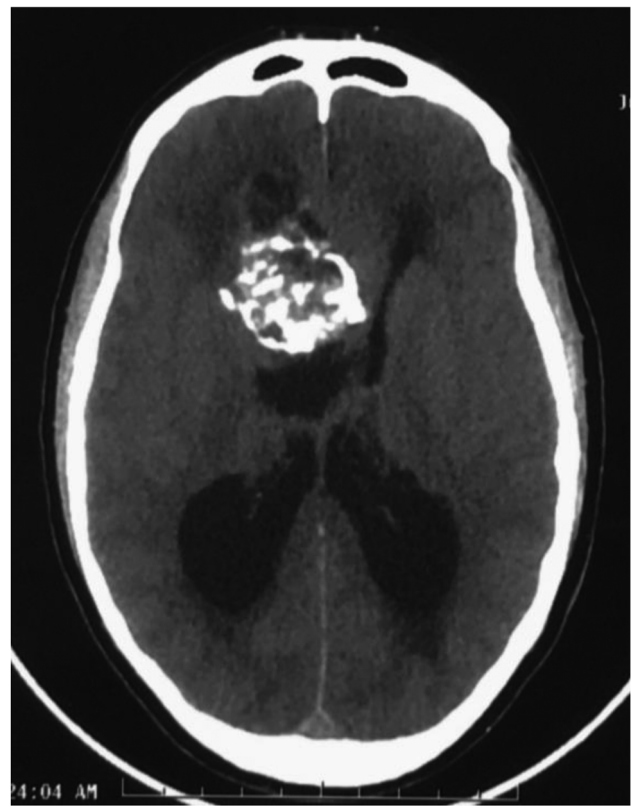


Figure 3. Non-contrast computed tomography revealing a calcified cystic structure in the suprasellar region, accompanied by hydrocephalus.

(nausea/vomiting, headache, visual abnormalities, endocrine dysfunction), radiological and imaging morphology, anatomical location of the tumor, its histological variant, tumor size, initial surgical treatment, complications of surgery, and adjuvant treatment, if any. As a retrospective observational study, ethical clearance from the institutional ethical committee of SKIMS was deemed unnecessary. Informed consent was obtained from all patients or their guardians.

Results

A total of 23 patients were studied over a period of five and a half years. The hospital-based incidence of the disease was found to be 0.061 per 100,000 population. Among the 23 patients, 13 (57%) were males and 10 (43%) were females (Table I and Table II), resulting in a male to female ratio of 1.3:1. The youngest patient in the study was 6 years old, and the eldest was 65 years old, with a mean age of 23 years. The majority of patients (39%) belonged to the age group of 10 to 18 years, followed by 17% in the age groups of 0 to 9 years, and 37 to 45 years, respectively.

In children, headache was the most common symptom, occurring in 75% of cases, followed by nausea/vomiting, which was reported in 50% of cases. In contrast, diminution

Table I. Sex distribution of the study population.

Sex	Frequency	Percentage
Male	13	57%
Female	10	43%
Total	23	100
p-Value	0.53	

Table II. Age distribution of the study population.

Age	Frequency	Percentage
0 to 9	4	17%
10 to 18	9	39%
19 to 27	3	13%
28 to 36	1	4%
37 to 45	4	17%
45 to 54	0	0%
55 to 63	1	4%
64 to 72	1	4%
Total	23	
Average	23 years	
Range	6 to 65 years	

Table III. Symptoms in various age groups.

Symptoms	Children (n=12)	Adults (n=11)	Total (n=23)
Nausea/Vomiting	6 (50)	3 (27)	9 (39)
Headache	9 (75)	5 (45)	14 (61)
Unsteadiness/Ataxia	1 (8)	1 (9)	2 (9)
Decreased level of consciousness	2 (17)	1 (9)	3 (13)
Nystagmus	2 (17)	1 (9)	3 (13)
Diminution of vision	5 (42)	6 (55)	11 (48)
Weakness	2 (17)	1 (9)	3 (13)
Failure to thrive	2 (17)	-	2 (9)
Hypogonadism	-	3 (27)	3 (13)
Duration of symptoms			
Mean (in months)	4.6	11.3	
Range	1 week to 10 months	1 week to 36 months	

of vision was the most common symptom among adults, affecting 55% of patients. Hypogonadism was exclusively present in adults, with a frequency of 27%. Children had a shorter duration of symptoms before presentation (mean of 4.6 months) compared to adults (mean of 10.3 months) (Table III).

Comorbidities (Table IV) were present in 26% of the population, including hypertension (13%), hypothyroidism (9%), and diabetes mellitus (4%). A suprasellar component was observed in the majority of cases, with 92% in children and 81% in adults (Table V). Cystic tumors were more common in children (58%), whereas mixed cystic and solid components were more common in adults (45%). Solid tumors were the least common, seen in 17% of all patients (Table VI).

Surgery was the primary mode of treatment for 22 out of 23 patients, with 41% undergoing gross-total resection and 59% undergoing sub-total resection (Table VII). Five patients required a shunting procedure before definitive surgery to relieve hydrocephalus. The majority of surgeries (73%) were performed *via* a craniotomy approach, with the trans-nasal trans-sphenoid approach being used almost exclusively in adults (83%) (Table VIII) (Figure 4). One patient was managed conservatively due to their refusal for surgery.

Post-operative complications (Table IX) included diabetes insipidus (27%), cerebrospinal fluid leak (9%), meningitis (9%), diminution of vision (4.5%), and hydrocephalus (4.5%). One patient (4.5%) died in the post-operative period. The mean duration of hospital stay (Table X) postoperatively was 14 days, ranging from seven to 26 days. Most patients (68%) were discharged within two weeks, and 91% were discharged by three weeks.

Histological subtypes (Table XI) were mentioned for 17 out of 22 patients, with the adamantinomatous subtype seen in all children and the papillary subtype exclusively seen in

Table IV. Associated comorbidities of the study population.

Comorbidity	Frequency	Percentage
Hypothyroidism	2	9%
Hypertension	3	13%
Diabetes Mellitus	1	4%

Table V. Location of tumor as reported from radiology.

Location	Children	Adults	All ages
Intra-sellar	1 (8)	2 (18)	3 (13)
Supra-sellar	3 (25)	4 (36)	7 (30)
Both	8 (67)	5 (45)	13 (57)
Total	12	11	23

adults (80%). Five patients did not have a histological subtype mentioned. Adjuvant therapy (Table XII) in the form of radiotherapy was administered to 55% of patients (12 out of 22).

Discussion

Craniopharyngiomas present a multifaceted clinical and epidemiological landscape, which our study sought to illuminate through an extensive examination conducted at Sher-i-Kashmir Institute of Medical Sciences Srinagar. By amalgamating retrospective data analysis with prospective observations, we endeavored to unravel the intricacies surrounding this rare intracranial tumor.

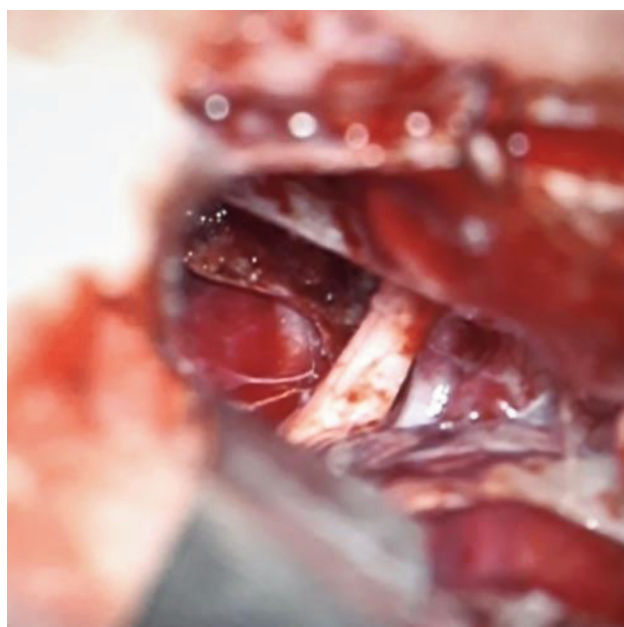


Figure 4. Intraoperative photograph depicting the classical pterional or sub-frontal route. Limitations include the optic nerves/optic chiasm usually lying in front of the tumor, thereby restricting the surgical window.

A fundamental aspect of craniopharyngioma epidemiology lies in its age distribution, which exhibits a distinct bimodal pattern characterized by peaks in childhood and late adulthood. Our findings echoed this pattern, with the mean age at presentation being 23 years, ranging from 6 to 65 years. Noteworthy clusters were evident in the age groups of 10 to 18 years, 0 to 9 years, and 37 to 45 years, aligning with established literature (2, 4, 5). This bimodal distribution underscores the importance of age stratification in understanding the disease trajectory and tailoring management strategies accordingly.

Sex distribution is another pertinent aspect, with prior studies indicating no significant difference in craniopharyngioma incidence between males and females (2, 4, 5). Consistently, our study demonstrated near parity in sex representation, with males comprising 57% and females 43% of the cohort. This sex neutrality suggests that craniopharyngioma development may not be influenced by sex-specific factors but rather by broader demographic and physiological determinants. Clinical presentation offers invaluable insights into the diverse symptomatology associated with craniopharyngiomas, which varied between pediatric and adult patients in our study. While headache emerged as the predominant symptom overall, its frequency differed between age groups, with children predominantly presenting with headache (75%) and nausea/vomiting (50%), whereas adults more commonly exhibiting diminution of vision (55%) and

Table VI. Consistency of tumor as reported from radiology.

Consistency	Children	Adults	Total
Purely or predominantly cystic	7 (58)	3 (27)	10 (43)
Mixed	4 (33)	5 (45)	9 (39)
Purely or predominantly solid	1 (8)	3 (27)	4 (17)
Total	12	11	23

Table VII. Extent of tumor resection.

Extent of resection	Children	Adults	All ages
Gross-total	5 (42)	4 (40)	9 (41)
Sub-total	7 (58)	6 (60)	13 (59)
Total	12	10	22

Table VIII. Surgical approach undertaken for tumor resection.

Surgical approach	Children	Adults	All ages
Craniotomy	11 (92)	5 (50)	16 (73)
Trans-sphenoid	1 (8)	5 (50)	6 (27)
Total	12	10	22

hypogonadism (27%). This nuanced variation underscores the need for age-specific diagnostic and management protocols (11-13, 27, 28). Radiographic imaging provided further elucidation, revealing a predilection for suprasellar localization and varied tumor consistency between pediatric and adult cohorts. While children tended to present with predominantly cystic tumors, adults exhibited tumors with mixed consistency. This heterogeneity underscores the complex pathophysiology of craniopharyngiomas and necessitates tailored therapeutic approaches to address diverse tumor characteristics (9, 29-32). Surgical intervention remains the cornerstone of treatment, with the majority of patients undergoing either gross-total or sub-total resection, predominantly *via* a craniotomy approach. Notably, the choice of surgical approach varied based on tumor characteristics, with purely intra-sellar tumors typically addressed *via* a trans-sphenoid approach. Despite advancements in surgical techniques, post-operative complications were observed, including diabetes insipidus, cerebrospinal fluid leak, meningitis, diminution of vision, and hydrocephalus, underscoring the challenges inherent in managing these complex tumors (16, 27, 31, 32). Histological analysis revealed distinct subtypes, with the adamantinomatous subtype predominating in children and the papillary subtype in

Table IX. Common complications after surgery.

Complications	Frequency	Percentage
DI (transient or permanent)	6	27%
CSF leak	2	9%
Meningitis	2	9%
Diminution of vision	1	4.5%
Hydrocephalus/Shunt blockage	1	4.5%
Mortality	1	4.5%

Table X. Duration of hospital stay.

Period of hospital stay	Number of patients
Up to 1 week	1
7-14 days	12
15-21 days	8
22-28 days	2
Average	14

adults. This corroborates previous studies and underscores the importance of histopathological characterization in guiding treatment decisions and prognostication (33-35). Adjuvant radiotherapy emerged as a critical adjunctive therapy, particularly in cases of incomplete resection or tumor recurrence, contributing to long-term disease control. Modern radiation therapy technologies offer enhanced precision and reduced morbidity, promising improved treatment outcomes and patient prognosis (36-39).

Role of radiotherapy in craniopharyngiomas. The role of radiotherapy in the management of craniopharyngioma (CP) is a subject of ongoing debate and scrutiny, primarily due to the tumor's sharp, irregular borders and its propensity to adhere to vital neurovascular structures, rendering surgical interventions potentially hazardous (40). Nevertheless, it is generally recommended that radiotherapy be administered following incomplete excision of a craniopharyngioma (40). Moreover, radiotherapy serves as an integral component of the multidisciplinary management approach for patients with incompletely resected or recurrent craniopharyngioma, offering favorable long-term disease control with limited toxicity (41). Radiotherapy plays various roles in the management of craniopharyngioma, including tumor shrinkage before surgery and postoperative application in cases of subtotal resection (STR) or tumor recurrence (42). In rare instances where complete surgical removal is unfeasible, radiotherapy may serve as the sole treatment modality (43). Studies indicate that radiotherapy achieves long-term disease control comparable to

Table XI. Histological variants in children, adults, and the whole group.

Histology	Children	Adults	Total
Adamantinomatous	8 (67)	1 (10)	9 (41)
Papillary	0 (0)	8 (80)	8 (36)
Craniopharyngioma not-specified	4 (33)	1 (10)	5 (23)
Total	12	10	22

Table XII. Adjuvant therapy.

	Frequency (n=22)	Percentage
Irradiated	12	55%
No adjuvant therapy	10	45%

radical surgery alone, making it a cornerstone in the therapeutic armamentarium for craniopharyngioma (42).

Notably, radiotherapy alone, without surgical intervention, may be suitable for select patients with craniopharyngioma, thereby mitigating the risks associated with surgery (43). Evidence suggests that the use of radiotherapy following incomplete craniopharyngioma resection significantly enhances recurrence-free survival rates by 75-90%, obviating the need for repeat surgery and its associated morbidity and mortality (44). Moreover, excellent disease control and functional outcomes are attainable with radiotherapy alone in appropriately selected patients (43).

Traditionally, external radiotherapy has been the preferred modality, although recent advancements have introduced alternative approaches, such as cavitary radiation and stereotactic radiosurgery (SRS), which have demonstrated efficacy in tumor control (42). However, radiotherapy is not without risks, as it may disrupt the hypothalamic-pituitary axis, leading to complications, such as diabetes insipidus, panhypopituitarism, hypogonadism, hypothalamic obesity, and sleep disturbances (42). Additionally, radiotherapy can impact cognitive function and carries the risk of secondary malignancies, radiation necrosis, vasculopathy, and neurodegenerative effects (42).

Given the potential impact on neurological, endocrine, and cognitive function, careful evaluation of these factors is imperative in guiding treatment decisions, particularly in pediatric patients with craniopharyngioma (45). Modern radiation therapy technologies, including fractionated 3-D conformal radiotherapy, fractionated stereotactic radiotherapy, stereotactic radiosurgery, intensity-modulated radiation therapy, and proton therapy, offer precise target identification and delivery, enhancing treatment efficacy and minimizing adverse effects (42, 46).

In conclusion, radiotherapy plays a pivotal role in the comprehensive management of craniopharyngioma, offering effective disease control and mitigating the risks associated with surgical interventions. However, careful patient selection and meticulous evaluation of treatment-associated risks and benefits are essential to optimize therapeutic outcomes and preserve patient quality of life.

Conclusion

Craniopharyngiomas present a multifaceted clinical and epidemiological profile, as elucidated by our comprehensive analysis. The bimodal age distribution underscores the importance of age-specific management strategies, while near sex parity suggests a lack of sex-specific factors in tumor development. Clinical presentations vary between pediatric and adult patients, highlighting the need for tailored diagnostic and therapeutic approaches. Radiological characteristics, including tumor localization and consistency, further underscore the heterogeneity of craniopharyngiomas and the necessity for individualized treatment strategies. Surgical resection remains the cornerstone of treatment, although post-operative complications necessitate careful management. Histological subtypes provide valuable prognostic information, guiding treatment decisions and predicting outcomes. Adjuvant radiotherapy plays a crucial role, particularly in cases of incomplete resection or tumor recurrence, offering long-term disease control with limited toxicity. Overall, our study contributes to a deeper understanding of craniopharyngiomas, informing clinical practice and guiding therapeutic interventions to improve patient outcomes in this challenging clinical scenario. Further research is warranted to explore emerging treatment modalities and optimize therapeutic strategies for craniopharyngioma management.

Conflicts of Interest

The Authors declare that they have no competing interests in relation to this study.

Authors' Contributions

Conceptualization, A.M., M.F. and A.R.B.; Methodology, A.F.A.H.; Software, A.F.A.H., F.A.M. and A.K.; Validation, G.F., G.E.U., G.S. and B.C.; Formal analysis, A.M., M.F. and A.R.B.; Investigation, A.F.A.H.; Resources, F.A.M. and A.K.; Data curation, G.S.; Writing – Original draft preparation, A.M., M.F., G.F. and G.S.; Writing – review & editing, G.F., G.E.U., G.S. and B.C.; Visualization, G.F., G.E.U., G.S. and B.C.; Supervision, G.F., G.E.U., G.S. and B.C.; Project administration, B.C.; All the Authors have read and approved the manuscript.

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