Collage of Health Science

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PREDICTORS OF TREATMENT OUTCOMES IN PATIENTS WITH CRANIOPHARYNGIOMA SURGICALLY TREATED AT TWO TEACHING HOSPITALS IN ADDIS ABABA ETHIOPIA: A 10 YEAR RETROSPECTIVE COHORT STUDY FROM JAN 2013- JAN 2023

A Thesis to be submitted to the Department of Surgery as a partial fulfilment of Specialty Certificate in Neurosurgery

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Abstract

Background: Craniopharyngioma is a rare disabling disease due to its malignant behavior though it's histologically benign. The bulk of literatures that describe treatment strategies and treatment outcomes of patients with craniopharyngioma are from westerns and the long term neurological, endocrinological, ophthalmological and psychosocial outcomes are not well studied in developing countries.

Objective: The aim of this study was to assess neurological, ophthalmological, endocrinological and overall functional outcomes of patients with craniopharyngioma at TASH and MCM comprehensive specialized hospitals from Jan 2013 to Jan 2023.

Methodology: Retrospective cohort study was conducted to assess the predictors of treatment outcome of patients with craniopharyngioma was undertaken at TASH and MCM hospitals in Addis Ababa, Ethiopia which are affiliated Neurosurgical hospitals. The long term neurological, ophthalmological, endocrinologic and general functional outcomes of patients treated for the past 10 years from Jan 2013 to Jan 2023 was studied. Data was collected by chart review and via phone contact to the patients. The MRI/CT image was re-evaluated when available. The neurological, ophthalmological, endocrinological and overall functional outcomes were analyzed. The functional independence and Craniopharyngioma clinical status scale (CCSS) was used to assess the overall functional status of patients. Factors affecting the functional outcome were identified and correlations were performed using SPSS Version 25.

Results: Among 40 patients included in the study headache (95%, 38/40), visual deterioration (87.5%, 35/40) and lethargy (85%, 34/40) were the most common presentations. Thyroxine and cortisol were the most deficient hormones preoperatively (35%, 14/40) and (32.5%, 13/40) respectively. Pre operative DI was present in 35% of the patients. Craniotomy was done in (70 %, 28/40) and trans nasal surgery for (22.5%, 9/40) of patients, VPS for (5%, 2/40) and EVD for (2.5%, 1/40) patients. STR was done in (60%, 24/40) and GTR in (20%, 8/40) patients. Based on craniopharyngioma clinical status scale, 40% (16/40) of patients have sever neurologic deficit,

42.5% (17/40) of patients have bilateral blindness, 25% (10/40) have DI and panhypopituitarism, 45% (18/40) of patients have post operative obesity and 60% (24/40) of patients are entirely dependent on others for self-care. The mortality rate was 47.5% (19/40). There was statistically significant association between tumor epicenter, tumor size, brain stem involvement, HCP, meningitis, dysnatremia, length of hospital stay and length of ICU stay with poor functional outcome.

Conclusion: Craniopharyngioma is associated with very high rate of mortality rate in our setup and higher grade of hypothalamic involvement and signs of increased ICP at presentation are predictors of mortality. Majority of the survivors have also significant ophthalmologic, neurologic and endocrinologic morbidities.

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ACRONYM

AAU	Addis Ababa University
CNS	Central Nervous System
CP	Craniopharyngioma
CSF	Cerebro Spinal Fluid
DI	Diabetes Insipidus
EEA	Endonasal Endoscopic Approach
EES	Endonasal Endoscopic Surgery
GH	Growth Hormone
GTR	Gross Total Resection
ICP	Intra Cranial Pressure
MCM	Myungsung Christian Medical
RT	Radiotherapy
SPSS	Statistical Package for Social Sciences
STR	Sub Total Resection
TASH	TikurAnbessa Specialized Hospital
WHO	World Health Organization

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1. INTRODUCTION

1.1 Back ground

Craniopharyngioma is a rare disabling disease that arises from squamous epithelial cells in the remnant of Rathke pouch. (1-7). They represent 2-5% all CNS tumors and 6-8% of pediatric brain tumors. (4, 7-9). A 5-year retrospective study by Damtie et.al in Tikur Anbessa specialized hospital in Addis Ababa showed that craniopharyngioma was the third most common pediatric brain tumor after medulloblastoma and astrocytoma comprising 12.1%. (10). Its histologically benign tumor of WHO- grade 1 but it is well known for its aggressive behavior due to its close proximity to the vital neurovascular and endocrine structures including the optic apparatus, pituitary stalk and gland, circle of willis, hypothalamus and the 3rd ventricle making both treatement and treatment related complications unacceptably high and difficult to manage. (6, 8). Craniopharyngioma has two histological subtypes; adamantinomatous and papillary types. Adamantinomatous craniopharyngiomas are more common in children but can also affect adults too but papillary sub type is exclusively present in adults. (4). It can affect all age groups; but the peak incidence has a bimodal distribution; the 1st peak between 5-15 years and the 2nd between 45-60 years old. (6,7).

The presentation of patients with craniopharyngioma is variable and depends on the location, size, tumors histologic sub type and the patients age group. The symptoms are often due to mass effect or infiltration on the adjacent structures and include hormonal and hypothalamic dysfunction, visual deficits, behavioral disturbance and hydrocephalus. (2, 3) . Treatment of craniopharyngioma is challenging because of both substantial treatments related co morbidities and the optimal treatment and extent of resection is always a matter of debate. (5, 7-9, 19-23) Surgical resection is considered as the primary treatment modality for craniopharygiomas especially in children due to the long-term deleterious effect of radiation therapy. (24, 25)

To date the variable prognostic factors of craniopharyngioma are not well established and couldn't find consistent data about the prognosis of these patients. (32) Craniopharyngioma patients have decreased survival with an increased mortality rate by 3-6 folds higher than the general population and the overall 10-year survival rate ranges from 83%-93%. (36) The deaths

are not solely attributed to the tumor and the surgical intervention but there is an added burden of mortality associated with long term cardiovasculr, cerebrovascular, and respiratory complications. (7). The recurrence of craniopharyngioma is common with reported incidence of 9-62%. (9.40)

The current trend in management of craniopharyngioma favors conservative approach in conjunction with radiotherapy due to serious neurocognitive sequelae and reduced quality of life and increased morbidity and mortality associated with the traditional radical resection. (3, 47)

1.2 Statement of the problem

Craniopharyngioma is a relatively rare histologically benign tumor 2-5% all CNS tumors and 6-8% of pediatric brain tumors. (1-9). It was the third most common pediatrics brain tumor after medulloblastoma and astrocytoma which accounts for 12.1 % of brain tumors in a 5-year retrospective study at TASH. (10) Though it is biologically benign, craniopharyngioma is well known for its aggressive behavior due to its close proximity to the vital neurovascular and endocrine structures including the optic apparatus, pituitary stalk and gland, circle of willis, hypothalamus and the 3rd ventricle making both treatement and treatment related complications unacceptably high and difficult to manage. (6, 8). The optimal treatment for craniopharyngiomas is not well defined. Surgical resection is considered to be the primary treatment modality for craniopharygiomas especially in children but the extent of resection is not uniformly agreed upon and is always a matter of debate. (24-25). The current trend in the management of craniopharyngioma is towards conservative managemet i.e., STR with radiation therapy. (. (5, 6, 28, 29). But this approach is at the expense of tumor recurrence and it is evident that treatment of recurrent craniopharyngioma is even more challenging. From the previous study in this institution (10), it is fair to say craniopharyngioma may not be uncommon in our set up. When the above-mentioned treatment challenges are considered in resource limited countries like Ethiopia, the problem is really worrisome. Here in our set up we have only limited options of management mainly of surgical resection and or ommaya insertion. But the extent of resection and its effect on complications and long-term outcome is not yet studied. The other challenge to go for STR with radiotherapy in the management of craniopharyngioma in resource limited countries especially in Ethiopia is the unavailability of sufficient radiation center. Till recently, there is only one radiation center all over the country to over radiotherapy for all types of tumors that need radiation which is difficult to think like it is safe to do subtotal and irradiate. And as expected the waiting list for radiation is unacceptably high.

Hormonal deficiency is one of the major problems of craniopharyngioma which is common both preoperatively and post operatively as treatment complication. In some studies, preoperative hormonal deficiency is reported in as high as 90% of the cases. (7, 9). This is a bad fact in the developing countries like Ethiopia where the majority of patients could not afford for replacement therapy and the financial constraints with which our patients face is an obstacle to have long term follow-up. Not only treatment costs but also imaging studies and laboratory

investigations to look for the complications of craniopharyngioma are also costly which add up for the loss of patients from long term follow-up but this needs future analysis of economic burden of craniopharyngioma on long term follow up of patients. It is the intention of this study to assess the neurological, ophthalmological, endocrinological and overall functional outcomes of patients with craniopharyngioma treated in our set up as there is no similar study done previously. Patients with craniopharyngioma have decreased survival with an increased mortality rate by 3-6 folds higher than the general population (36) and the deaths are partly attributed to long term cardiovasculr, cerebrovascular, and respiratory complications (7); Hence it is fairly rational to study the long-term outcome of these patients.

1.3 significance of the study

The long term neurologic, ophthalmologic and endocrinologic as well as the overall functional outcome of patients with craniopharyngioma is not studied in Ethiopia. It is clear that a standard institutionally based treatment protocol and follow-up schedule is paramount to pick the complications timely and treat accordingly in this difficult neurosurgical problem and this research will provide valuable input for such purpose. This study will also serve as a landmark on which future prospective studies will be done.

2. LITERATURE REVIEW

Craniopharyngioma is a rare disabling disease that arises from squamous epithelial cells in the remnant of Rathke pouch. (1-7). They represent 2-5% all CNS tumors and 6-8% of pediatric brain tumors. (4, 7-9). A 5-year retrospective study by Damtie et.al in Tikur Anbessa specialized hospital in Addis Ababa showed that craniopharyngioma was the third most common pediatric brain tumor after medulloblastoma and astrocytoma comprising 12.1%. (10).

It can affect all age groups; but the peak incidence has a bimodal distribution; the 1st peak between 5-15 years and the 2nd between 45-60 years old. (6,7). Craniopharyngiomas commonly arise from suprasellar region though they may originate in other locations like sella, parasellar, pituitary gland, or the floor of third ventricle or may involve a combination thereof. (1-3, 5-7, 11)

The presentation of patients with craniopharyngioma is variable and depends on multiple factors. The symptoms are often due to mass effect or infiltration on the adjacent structures and include hormonal and hypothalamic dysfunction, visual deficits, behavioral disturbance and hydrocephalus. (2, 3) Headache and visual impairment are the two most common presentations of craniopharyngioma patients with reported frequencies of 50-78% and 47-87.5% respectively. (9, 13, 14) Signs and symptoms of increased ICP occur more frequently in children than adults whereas visual impairments are more common in adult patients with craniopharyngioma. (5, 9) Preoperative hormonal deficiency is diagnosed in substantial number of patients with some studies report in as high as 90% of the cases. (7, 9) As far as specific anterior pituitary hormonal dysfunction is concerned, GH deficiency is the most prevalent and most important hormonal deficiency in children which occurs in the range of 35-95%, 38 to 82% for follicle-stimulating hormone/luteinizing hormone, 21 to 62% for corticotrophin, and 21 to 42% for thyroid-stimulating hormone and between 6 and 38% of patients present with insufficient secretion of antidiuretic hormone and they may also present with neuromotor and psychiatric problems.(3-5) The histologic subtype of craniopharyngioma is also correlated with the clinical presentation of patients in which hypothalamic dysfunction and signs of increased ICP are more common in papillary craniopharyngioma whereas visuoendocrine disturbance is more common in adamantinomatous type. Neurocognitive deficits are more of a postoperative concern as they are subtle and overlooked preoperatively. (3)

Treatment of craniopharyngioma is challenging because of both substantial treatments related co morbidities and the optimal treatment and extent of resection is always a matter of debate. (5, 7-9, 19-23) Surgical resection is considered as the primary treatment modality for craniopharygiomas especially in children due to the long-term deleterious effect of radiation therapy. (24, 25) Different surgical options are available including total resection, subtotal resection (STR) with observation, STR with postoperative radiotherapy (RT), and cyst aspiration and/or biopsy followed by RT (external beam or intracavitary). (21) There are two main schools of thoughts on how aggressive the surgery should be and on the role of post operative radiotherapy. (21, 26) One group of scholars think that GTR offers long term survival by decreasing recurrence with additional surgical procedures and its associated morbidity and it eliminates the need for radiotherapy with its deleterious side effect. Others think that the close proximity and usual involvement of critical neurovascular and endocrine structures makes GTR to be associated with unacceptable morbidity and recommend STR with adjuvant radiotherapy. (26) On the other hand, the study conducted on 284 patients by Xiang-en Shi et al. showed that the mortality, morbidity, and recurrence rate in patients received total resection are lower than those of patients underwent subtotal or partial resections. (23) For many years GTR was considered to be the primary goal of surgery in craniopharyngioma and this was the preferred treatment objective by the American Pediatric Neurosurgeons in 1990s as described by John H.Suh et al. (26, 27) Michael E. Sughrue and his colleagues conducted a systematic review on 540 patients who were surgically treated for craniopharyngioma showed that the overall rate of new endocrinopathy for all patients undergoing surgical resection was 37% and Patients receiving GTR had over 2.5 times the rate of developing at least one endocrinopathy compared to patients receiving STR alone or STR + XRT. The visual outcomes were worse in patients receiving XRT after STR compared to GTR or STR alone (GTR = 3.5% vs. STR 2.1% vs. STR + XRT 6.4%, $P = 0.11$. Ten percent of patients were left with panhypopituitarism.). (7, 10) Currently multidisciplinary and multi modal treatment approach is advocated in many centers because of the reduced quality of life associated with GTR and it is shown that the long-term overall survival and tumor control rate in both GTR and STR with radiotherapy are similar resulting the gold standard treatment for craniopharyngiomas is swinging away from radical surgical resection towards safe maximal resection with radiotherapy. (5, 6, 28, 29) But in the

absence of randomized control trials evaluating the two main alternatives of craniopharyngioma management, it is still difficult to translate into clinical guidelines. (5)

Transcranial microsurgical approach was the traditional surgical management of craniopharyngiomas and trans sphenoidal surgery either microscopic or endoscopic approach is used recently for selected cases; to access small intrasellar or subdiaphragmatic tumors. Currently the endoscopic approach emerged as a credible surgical alternative to deal with suprasellar craniopharyngiomas and with advent of the techniques; almost all types of craniopharyngiomas can be a target for EEA. (4, 11) This is possible because of the many advantages of the EEA than transcranial approach in that the techniques of EEA is improved, the illumination is improved, they provide expansive view, provide direct access to pathology, reduce brain retraction and manipulation of the optic chiasm, and may decrease hospital stay and morbidity. (4) Nevertheless, the previously accepted concept of EES reserved only for sellar or small cystic suprasellar lesions has been challenged by several groups and, in experienced hands, is no longer valid. (7)

But the major problem with this approach is CSF leak which is difficult to manage ones happen. (11) A meta-analysis comparing outcomes in children with craniopharyngioma treated with transsphenoidal surgery to those treated with conventional transcranial surgery reported that transcranial surgery was associated with increased rates of diabetes insipidus, postoperative worsening of vision, and postoperative nonvisual neurological deficits. (8) A retrospective study on long-term outcomes for surgically resected craniopharyngiomas by John M. Duff et al. showed that Tumors initially treated via transsphenoidal approaches were associated with good outcomes compared with transcranial approaches. (33) Whether transcranial or endonasal approaches are better suited for the treatment of suprasellar craniopharyngiomas may depend on lesion characteristics, patient characteristics, and surgeon's preference. (7)

There are different transcranial approaches with their selection mainly depends on tumors location, extention and surgeons' preference. Anterolateral approache such as the pterional or an anterior approach such as the subfrontal approach are traditionally used to address prechiasmatic lesions. These approaches are also used to access lesions in subchiasmatic space. But for subchiasmatic

tumors with extensive invasion of the third ventricle the combination of pterional and transcallosal transventricular approaches is the best option. (7)

The timing and dose of radiotherapy after STR/biopsy is not well defined. 33 moon et al. compared the effect of early radiotherapy within 3 months of the initial surgery and the other group who received radiotherapy after progression or relapse and showed that overall survival and progression-free survival rates were similar, and visual acuity or field was better maintained, and DI was partly improved with early radiotherapy, but all deteriorated as the tumor progressed without early adjuvant radiotherapy. (35) This is supported by another systematic review on treatment-related morbidity and the management of pediatric craniopharyngioma by AAron J. ClArk and his colleagues. (6)

To date the variable prognostic factors of craniopharyngioma are not well established and couldn't find consistent data about the prognosis of these patients. (32) Craniopharyngioma patients have decreased survival with an increased mortality rate by 3-6 folds higher than the general population and the overall 10-year survival rate ranges from 83%-93%. (36) The deaths are not solely attributed to the tumor and the surgical intervention but there is an added burden of mortality associated with long term cardiovasculr, cerebrovascular, and respiratory complications. (7) Yaşargil et al. reported an intraoperative and early post operative mortality rate of 9.0% and the overall mortality rate was 16.7%. (37) Some of the important predictors of high mortality described in the literature include female sex, childhood onset, hydrocephalus, tumor recurrence, body mass index and panhypopituitarism. And majority of the long-term mortalities were attributed to metabolic disorders and cardiovascular complications. (9) Alberto M Pereira et al. reported the high incidence of long term cardiovascular neurologic and psychosocial morbidity with 22%, 49%, and 47%, respectively after treatment of craniopharyngioma. (36) Hypothalamic obesity is a feared complication especially in children and 40% of patients in Karavitaki et. al' s study is suffering from obesity. (28) Hypoythalamic injury also results in defective short-term memory, limited concentration spans and behavioral abnormalities, defective thirst sensation, and sleep disturbances. (12) The physical impairment and cognitive performance are the important aspects that determine the quality of life of patients with craniopharyngioma. Duff et al. conducted a retrospective analysis of 121 patients to study

the long-term outcome and showed that 60% of patients have good outcome in terms of functioning, vision, independent living, performance status, academic levels, work, and psychological status. (12, 33) Lethargy at presentation, visual deterioration, papilledema, tumor calcification, hydrocephalus, and tumor adhesiveness at surgery are some of the factors associated with poor outcomes. (33)

The recurrence of craniopharyngioma is common with reported incidence of 9-62%. (9.40) Hyun Joo Park et al. reported a 40% recurrence rate in his retrospective study of 64 patients. (38-41) The factors associated with increased recurrence rate include extent of resection, tumor biology, and adherence to critical neurovascular structures, hypothalamic involvement, and patient's age at presentation, lack of adjuvant radiation and duration of follow up. (9, 45-47)

The current trend in management of craniopharyngioma favors conservative approach in conjunction with radiotherapy due to serious neurocognitive sequelae and reduced quality of life and increased morbidity and mortality associated with the traditional radical resection. (3, 47)

3. Objective of the Study

3.1. General Objective

- To assess the neurological, ophthalmological, endocrinological and overall functional outcome of craniopharyngoma patients treated at TASH and MCM comprehensive specialized hospital from Jan 2013-Jan 2023

3.2. Specific bjective

- To identify predictors of treatment outcome in craniopharyngioma patients TASH and MCM comprehensive specialized hospital from Jan 2013-Jan 2023
- Identify the most common complications that occur after craniotomy for resection of craniopharyngiomas.
    - To determine the risk factors for these complications.
- To compare the rates of endocrine, neurologic, vascular, and visual complications
- To Describe the long-term outcomes
- To assess the recurrence rate and quality of life.

4. METHODOLOGY

4.1. Study area and period

The study was conducted in patients with craniopharyngioma treated from January 2013 to January 2023 . The study areas were TASH and MCM hospitals in Addis Ababa, Ethiopia which are affiliated Neurosurgical hospitals. TASH is the largest and government owned hospital in Ethiopia. It has around 700 beds out of which neurosurgical unit has 30 beds but currently the number of beds is significantly decreased due to re-innovation purpose. MCM is an affiliate hospital with a bed capacity of 169. Neurosurgical Service such as emergency and elective operations are done on a daily basis.

4.2. Study design

- A retrospective cohort study design was employed on treatment outcome of patients with craniopharyngioma who have been treated at TASH and MCM hospitals were studied

4.3 Population

All patients with craniopharyngioma treated at TASH and MCM hospital in the study period and full fill the inclusion criteria were studied.

4.4. Eligibility criteria

- INCLUSION CRITERIA

  Patients who were diagnosed and treated for craniopharyngioma at two hospitals: TASH and MCM.

  Histologically confirmed craniopharyngioma or typical radiological findings consistent with craniopharyngiom

  Patient who was having follow up for at least 1 year follow-up

- EXCLUSION CRITERIA:

  Patients with missed histological or radiological data

  Patients whose phone is not working and unable to have follow-up visit

4.5 Sample size and Sampling techniques

The sample size is calculated using Wang,X. et al sample size formula specific for our cohort study design considering visual symptoms as the strongest predictors of long term tumor recurrence rate and poor outcome in a retrospective study by Duff et al in which the recurrence rate was 15.1% with visual deterioration versus 9.1% without visual deterioration (P=0.024). (33, 48) The formula used to calculate based on proportion with 95% confidence interval and 80% desired level of power is:

$$n \text{ (each group)} = \frac{(p_0q_0+p_1q_1)\,(z_1\text{-}\alpha/2 + z_1\text{-}\beta)^2}{(p_1\text{-}p_0)^2}$$

Using this formula, the sample size is: $\frac{(0.09\text{x}0.9 +0.15\text{x}0.85)\,(1.96 +0.84)^2}{(0.15\text{-}0.09)^2} = 54.78 \approx 55$

Where: n- sample size in each group (Exposed and non-exposed)

p0: proportion of recurrence without visual deterioration=0.09

p1: proportion of recurrence with visual deterioration=0.15

q0: (1-p0) =0.9

q1: (1- p1) =0.85

z_1-α/2: 95 % confidence interval=1.96

z_1-β: 80% level of power=0.84

4.6 Study variables

- Dependent Variables
  - Different complications (Neurological, endocrinopathies, visual deteriorations and vascular complications)
  - Recurrence rate

        - Quality of life
    - Independent Variables
        - Age
        - Sex
        - Clinical symptoms and signs
        - Preoperative endocrinopathies
        - Preoperative imaging findings: size, location, cystic vs solid, HCP, Pugets grade …
        - Histologic subtype
        - Treatment modalities
        - Extent of resection

4.7. Data collection and procedure

A structured questionnaire was prepared by the principal investigator and a standard patient reported outcome measurement tool was used

- Patients' charts were retrieved and basic demographic, endocrine, metabolic, ophthalmological, and neurological data were collected from medical documentation at the time of diagnosis, after the surgical procedure, and at the last follow-up
- When available, the preoperative MRI was re-evaluated to assess the association between the tumor characteristics and outcome of patients with craniopharyngioma. The presence of hydrocephalus, calcification, enhancement pattern, solid and cystic component, and hypothalamic tumor involvement according to the Puget grading was assessed and the most recent follow-up imaging was studied to assess for post operative sequelae and to evaluate recurrence.
- All alive patients were invited for a follow-up visit and those who couldn't came for follow up visit were contacted via phone call so as to evaluate the additional long-term endocrine, metabolic, and neuropsychiatric conditions.
- The overall functional status of the patients was assessed based on the cranipharyngioma clinical status scale and using wen et al. functional classification scale through phone call or in person for those who were able to come for follow-up visit.

4.8. Data processing and Analysis

- The collected data were coded and entered into IBM SPSS version 25.0 software for analysis. Categorical variables were described as numbers and percentages and continuous variables in mean and standard deviations. For the descriptive statistics we use 95% confidence interval. Chi-square or Fishers exact test was used to compare proportions for categorical variables and continuous variables were compared by using correlational analysis with pearson's correlation coefficient. Variables that have association on Chi-square test or Fishers exact test and on correlational analysis were subjected to linear and multivariate regression analysis to assess the strength of the associations. Differences with a p value of <0.005 were considered statistically significant.

4.9. Data quality assurance

- The questionnaires are developed after reviewing relevant literatures to the subject include all the variables that address the objective of the study. Pretest will be conducted on five percent of the sample and appropriate modification will be done. The principal investigator will have frequent contact with the advisors during data collection and data processing and check for the quality of the data.

4.10 Ethical Consideration

- Written informed consent will be taken from patients who are willing to have further follow-up visit with the principal investigator.
- The study will be conducted after getting Approval and ethical clearance from the Institutional Review Board (IRB).
- The participants' information shall be kept confidentially. The investigator is responsible for ensuring the confidentiality and keeping the documents discreetly.

4.11. Operational definition

- Long term follow-up: patients with craniopharyngioma having follow-up for more than one year
- Panhypopituitarism: craniopharyngioma patients with more than 3 hormonal dysfunctions
- GTR: >95% removal of the lesion leaving calcified remnants on the stalk/hypothalamus

- STR: detection of residual tumor on post operative imaging and/ or neurosurgeons report of incomplete excision
- Biopsy: Endoscopic cystic puncture for HCP and taking sample for diagnosis or in the form of stereotactic surgery

5. Results

Sociodemographic Characteristics

A total of 63 patients with craniopharyngioma were treated in the study period at TASH and MCM surgically out of which 40 patients fulfil the inclusion criteria, 77.5% (31/40) from TASH and22.5% (9/40) patients from MCM hospitals. Among 40 patients included in the study 55% (22/40) are males and 45% (18/40) are females. Regarding age, 55% (22/40) of patients are adults and 45% (18/40) were pediatrics patients with the mean age of presentation was 24 years old. The marital status of the patients is that 57.5% (23/40) of patients were not married while 42.5% (17/40) of patients have married.

Clinical Presentation

Headache (95%, 38/40), visual deterioration (87.5%, 35/40) and lethargy (85%, 34/40) were the three most common presentations. Fifty-five percent of patients (22/40) had signs of increased ICP like vomiting which was correlated with hydrocephalus. The other symptoms are described on table 1. The duration of visual deterioration ranges from two weeks to more than 2 years with the mean presentation being 7.4 months. And it was bilateral in (85. 7%, 30/35) and unilateral in (14.3%, 5/35). Bitemporal hemianopsia was the most common clinical finding found in (60%, 24/40) of patients while 22.5% (9/40) patients didn't have light perception on presentation. On pre-operative ophthalmologic assessment, optic atrophy was identified in (62.5%, 25/40) of patients and hemiparesis was present in (17.5%, 7/40) of patients. Polyuria and polydipsia were present in 9 patients (22.5%) and 12 patients (30%) were short stature at presentation. In the reproductive age group 5 patients (12.5%) were amenorrheic and there was sexual dysfunction in 3 patients (7.5%).

Pre-operative endocrinologic assessment revealed pre operative DI and Thyroxine deficiency were the most common abnormalities identified in 14 patients (35%) followed by cortisol deficiency in 13 patients (32.5%). Though 30 % of the patients had short stature, GH deficiency was present in (12.5%, 5/40); the GH status was not known in the majority of patients (65%, 26/40).

Table 1: Sociodemographic and Clinical Presentation, Physical Findings, Pre-operative endocrinopathies in patients with craniopharyngioma treated at MCM and TASH from Jan 2013-2023

Demographics	Frequency	Percent
Mean age at Dx	24	
Pediatrics <18	18/40	45
Adult >18	22/40	55
Sex		
Male	22/40	55
Female	18/40	45
Marital Status		
Married	17/40	42.5
Not married	23/40	57.5
Symptoms		
Headache	38/40	95
Vomiting	22/40	55
Seizure	8/40	20
Visual deterioration	35/40	87.5
Lethargy	34/40	85.0
Short stature	12/40	30.0
Sexual dysfunction	3/22	13.6
Polyuria/polydipsia	9	22.5
Physical Findings		
Visual Acuity	Rt-N(%)	Lt-N(%)
NLP	10 (25.0)	16(40.0)

HM	2 (5.0)	1(2.5)
1m	1 (2.5)	7(17.5)
3m	6 (15.0)	5(12.5)
6m	7 (17.5)	11(27.5)
Visual Field cut	23	57.5
Optic Atrophy	25	62.5
Papilledema	14	35.0
Hemiparesis	7	17.5
Pre-operative		
Endocrinopathies		
GH deficiency	5	12.5
Thyroxine deficiency	14	35.0
Cortisol deficiency	13	32.5
Sex hormone deficiency	7	17.5
PRL deficiency		
Pre operative DI	14	35.0

Upon evaluation of preoperative MRI and or CT scan of the patients, the mean tumor size was 4.58 cm (2-9 cm, SD, 1.56). The epicenter of the tumor was suprasellar in 27 patients (67.5%) and in 97.5% (39/40) of the tumors had variable degree of contrast enhancement. Calcification was evident in 34 patients (85%) and its morphology is mainly cystic in 55% (22/40) of the cases. Hypothalamic involvement was assessed based on Puget's grading score and 23 patients (57.5%) had Puget grade 2 involvement, 10 patients (25%) grade 1 and 7 patients (17.5%) grade 0 hypothalamic involvement. Hydrocephalus was present in 21 patients (52.5%) out of which pre operative CSF diversion was done for 13 patients (61.9%). Third ventricle, optic nerve involvement, tumor's extension and the its mass effect are presented in table 2.

Table 2: Pre operative imaging findings of patients with craniopharyngioma treated at MCM and TASH from January 2013-2023

Tumor characterstics	Frequency	Percent
Mean tumor size	4.58 cm (2-9 cm, SD, 1.56)	
< 3cm	6	15.0
3-6 cm	26	65.0
>6 cm	8	20.0
Tumor Epicenter		
Sellar	8	20.0
Supra sellar	27	67.5
Third ventricle	2	5.0
Multicompartmental	3	7.5
Tumor consistency		
Mainly cystic	18	45.0
Both cystic and solid	22	55.0
Calcification	34	85.0
Enhancement	39	97.5
Sellar floor erosion	14	35.0
Extensions		
Sub frontal	9	22.5
Middle fossa	8	20.0
Posterior fossa	12	30.0

Hypothalamic Involvement		
Puget grade 0	7	17.5
Puget grade 1	10	25.0
Puget grade 2	23	57.5
Pre operative HCP	21	52.5
Third ventricle involvement	24	60.0
Vascular encasement	9	22.5
ICA	4	10.0
MCA	2	5.0
ACA	1	2.5
BA	2	5.0

Treatment modalities and complications

Craniotomy and or TSS was done in 37 patients (92.5%); (craniotomy for 28 patients and TSS for 9 patients) and VPS was done for two patients and EVD was done for 1 patient. Among the surgical approaches, pterional craniotomy was the most common approach used in 25 patients (62.5%) and trans nasal approach was used in 9 patients (22.5%). Regarding the extent of resection, GTR was attained only in 8 patients (20%) and STR was in 24 patients (60%). The most common reason for STR was hypothalamic involvement in 7 patents (29.1%) followed by vascular incasement in 6 patients (25%). There was intra operative major vascular injury in 2 patients (5%). The pathology was adamantinomatous in 29 patients (72.5%) and papillary in 4 patients (10%). It is unknown in 17.5 % patients (7/40).

Dysnatremia was the most common complication identified in 23 patients (57.5%) out of which hypernatremia in 20 patients (50%) and hyponatremia 3 patients (7.5%). Nine patients (22.5%)

were complicated by meningitis, brain abscess in 4 patients (10%) and other HAI was identified in 8 patients (20%). Five patients (12.5%) were complicated with CSF leak.

Post operative DI was found in 72.5 % of patients (29/40) out of which 44.8% was transient (13/29) and 55.2% was permanent.

Table 3: Treatment modalities and Complications in patients with craniopharyngioma treated at MCM and TASH from January 2013-January 2023

Treatments given	Frequency	Percent
Surgery	37	92.5
VPS	2	5.0
EVD	1	2.5
Treatment of HCP		
Definitive surgery	8	20.0
VPS	13	32.5
EVD	1	2.5
Surgical Approach		
Pterional	25	62.5
Combined pterional and sub frontal	3	7.5
Trans nasal	9	22.5
EOR		
GTR	8	20.0
STR	24	60.0
Biopsy and cystic fenestration	5	12.5
Pathology		
Adamantinomatous	29	72.5
Papillary	4	10.0
Unknown	7	17.5
Complications		

Vascular Injury	2	5.0
CSF leak	5	12.5
Meningitis	9	22.5
Brain abscess	4	10.0
Other HAI	8	20.0
Dysnatremia	23	57.5

Functional Outcome and Mortality

Based on the craniopharyngioma clinical status scale, 16 patients (40%) had sever neurological deficit, 4 patients (10%) had moderate deficit (mild hemiparesis and independent ambulation or moderately controlled seizure), 10 patients (25%) had mild deficit (CN palsy or well controlled seizure), and 10 patients (25%) had no deficit**.** The duration of ICU stays (β-0.606, t-4.535, P-value <0.001) and the presence of vomiting /increased ICP (β-0.391, t-2.93, P-value: 0.007) are statistically significant associations that affect the neurological outcome in multivariate analysis.

The visual outcome based on CCSS is that 17 patients (42.5%) had bilateral blindness, 4 patients (10%) had unilateral blindness/homonymous hemianopsia, 12 patients (30%) had mild acuity deficit/field cut and normal visual acuity and visual field in 7 patients (17.5%). Compared from the pre operative visual assessment, the vision was improved in 10 patients (25%), worsened in 9 patients (22.5%) and remained the same in 25 patients (52.5%). With multiple linear regression analysis, pre operative visual acuity has strong positive association (β -0.549, t-4.393, P-value <0.001), and length of ICU stays (β: -0.529, t: -4.234, P-value<0.001) and posterior fossa involvement (B: -0.367, t: -3.253, P-value: 0.004) has negative association with the visual outcome.

Regarding the endocrine outcome of patients based on CCSS, DI and panhypopituitarism was identified in 10 patients (25%), DI with or without mild anterior pituitary dysfunction was identified in 14 patients (35%), mild anterior pituitary dysfunction was found in 7 patients (17.5%) and 9 patients (22.5%) had normal anterior and posterior pituitary function. Pre operative DI has statistically significant positive association with post operative endocrinopathies

(β: 0.531, t: 4.078, P-value<0.001)) whereas the size of the tumor has a statistically significant negative association with post operative endocrinopathies in multivariate regression analysis (β: -0.269, t: -2.065, P-value:0.046)

Twenty-two patients (55%), had normal hypothalamic function based on CCSS, 11 patients (27.5%) have post op obesity without behavioral change and 7 patients (17.5%) had obesity with hyperphagia. Patients who have sellar floor erosion on imaging have statistically significant negative association with hypothalamic function (β: -0.562, t: -4.806, P-value <0.001) in multiple linear regression analysis. Unexpectedly there is no association with Puget's grade of hypothalamic involvement with post operative hypothalamic function (P-value:0.76 in Pearson chi-square test).

The educational and or employment status of patients based on CCSS was that 24 patients (60%) were completely dependent on others for self-care, 6 patients (15%) were behind in grade or don't maintain persistent employment and 10 patients (25%) had good academic performance and maintain persistent employment. With multivariate regression analysis the educational/employment status was strongly associated with visual field (P-value:0.011) and meningitis (P-value:0.001 with 95% CI).

The overall functional outcome was also assessed using Wen et al. measure of functional independence. We found 23 patients (57.5%) were entirely dependent on others for self-care, 5 patients (12.5%) were partially dependent, 8 patients (20%) were independent and 4 patients (10%) were grossly normal and independent. The factors that have statistically significant association with functional outcome on linear regression analysis includes post operative visual field (β-0.528, t-4.797, P-value<0.001), meningitis (β-0.288, t-2.897, P-value: 0.008), dysnatremia (β-0.278, t-2.749, P-value:0.011), and tumor size (β-0.227, t-2.124, P-value: 0.043).

The recurrence rate of patients in the study period was 5% (2/40). The mean follow-up period was 18.4 months (from 1 month-84 months).

Among 40 patients included in the study, 19 patients (47.5%) died. The factors that have statistically significant association with increased mortality identified on multivariate regression analysis are brain abscess (β -0.293, t-2.63, P-value: 0.014) HCP (β-0.326, t-2.145, P-value:

0.041), hypothalamic involvement (β-0.479, t-3.148, P-value-0.004) and dysnatremia (β- 0.299, t-2.586, P-value: 0.015).

Table 4: Functional outcome and Mortality of patients with craniopharyngioma assessed with craniopharyngioma clinical status scale and functional classification scale by Wen et al

		Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
		B	Std. Error	Beta	T	Sig.	Lower Bound	Upper Bound
1	**Functional Outcome**							
	Post op VF	.760	.158	.528	4.797	.000	.434	
	Meningitis	.817	.282	.288	2.897	.008	.237	
	Dysnatremia	.632	.230	.278	2.749	.011	.159	
	Tumor Size	.188	.088	.227	2.124	.043	.006	
2	**Death**							
	Hypothalamic involvement	.392	.125	.479	3.148	.004	.137	.647
	Brainabscess	.437	.166	.293	2.632	.014	.096	.778
	Dysnatremia	.264	.102	.299	2.586	.015	.054	.473

3.	**CCSS: Neurol**							
	ICUSW	.602	.133	.606	4.535	.000	.330	.874
	Vomiting	.966	.330	.391	2.930	.007	.291	1.641
4	**CCSS: Vision**							
	Preop VA	.112	.026	.549	4.393	.000	.060	.164
	ICU stay	-.218	.052	-.529	-4.234	.000	-.324	-.113
	PF Involvemn	-.871	.268	-.367	-3.253	.004	-1.426	-.316
5	**CCSS: Pituitary**							
	Pre op DI	3.196	.784	.531	4.078	.000	1.608	4.784
	Tumor size	-.496	.240	-.269	-2.065	.046	-.982	-.009
6	**CCSS: hypothalamic**							
	Sellar floor erosion	-.976	.203	-.562	-4.806	.000	-1.393	-.558
7	**CCSS: Educational**							
	Pre op VF	.566	.113	.629	5.001	.000	.334	.798
	Meningitis	.604	.221	.344	2.732	.011	.151	1.057

6. Discussion

Craniopharyngioma is a rare disabling disease that arises from squamous epithelial cells in the remnant of Rathke pouch. (1-7). They represent 2-5% all CNS tumors and 6-8% of pediatric brain tumors and is the third most common pediatric brain tumor after medulloblastoma and astrocytoma comprising 12.1% in our set up at Tikur Anbessa specialized hospital in Addis Ababa. (4, 7-9, 10). It can affect all age groups with peaks in two peaks, 1st peak between 5-15 and 2nd peak between 45-60 years old and in this study more than half of the patients (55%) are >18 years old with the mean age of presentation of 24 years old. (6, 7).

The majority of craniopharyngiomas have suprasellar epicenter with variable extensions to the parasellar, infra sellar growth or to the third ventricle. (. (1-3, 5-7, 11). In concert with these studies, the epicenter of the tumor was suprasellar in more than two-third of the cases (67.5%) but there was third ventricular involvement in 60% of the cases and posterior fossa/brain stem extension was identified in 30% of the patients.

The clinical presentation of patients is different affected by multiple factors including the age of the patient, tumor's epicenter and its extension, the size of the tumor and they usually present with a combination of hormonal and hypothalamic dysfunction, visual and neurologic symptoms. (2, 3). Headache and visual impairment are described the two most common symptoms of patients with craniopharyngoma with frequencies in between 50-78% and 47-87.5% respectively in the literatures. (5, 9). Likewise, Headache (95%, 38/40) and visual deterioration (87.5%,

35/40) are the two most common presentations of patients in this study followed by lethargy which occurred in 85% of patients (34/40).

Preoperative hormonal deficiency is diagnosed in substantial number of patients with some studies report in as high as 90% of the cases. (7, 9). GH deficiency is the most common endocrine abnormality which occurs in 35%-95% followed by follicle-stimulating hormone/luteinizing hormone in 38 to 82%. Corticotrophin deficiency occurred in 21 to 62%, and thyroid-stimulating hormone deficiency in 21 to 42% and between 6 and 38% of patients present with insufficient secretion of antidiuretic hormone and they may also present with neuromotor and psychiatric problems. (3-5). In this study, the most frequent hormonal deficiencies are thyroxine and ADH which occurs in 35% (14/40) of the cases each followed by cortisol deficiency which occurs in 13 patients (32.5%). Although GH stated as the most common hormonal deficiency in patients with craniopharyngioma in various literatures, it is not determined in 65% (26/40) of this study and only 12.5% (5/40) patients have GH deficiency. Mohammed J. Asha et al. demonstrates that the correlation of histopathology sub-type with specific clinical manifestation; patients with adamantinomatous craniopharyngioma present with visoendocrine disturbance while those with papillary type present with hypothalamic dysfunction and signs of increased ICP (3). This study fails to show this association.

Treating craniopharyngioma is a challenge due to its locally aggressive nature to the surrounding neurovascular structures and the co-morbidities following its surgical resection. And the extent of resection is yet to be defined. (5, 7-9, 19-23). The primary modality of treatment of craniopharyngioma is surgical resection specially in children to avoid the deleterious effect of radiation in the growing child. (24, 25)

Craniotomy and tumor resection and or ommaya insertion was done in 28 patients (70%) and microscopic/endoscopic TSS was done in 22.5% patients (9). GTR was achieved only in 20% patients (8/40) and STR in 60% of the cases, the remaining is either biopsy or cyst fenestration. A study conducted by Xiang-en Shi et al. in 284 patients showed that the mortality, morbidity, and recurrence rate in patients received total resection are lower than those of patients underwent subtotal or partial resections. (23). There is no statistically significant association identified in this study between the extent of resection and mortality (P-value:0.681) and extent of resection and recurrence (P-value: 0.986) on binary logistic regression analysis. Michael E. Sughrue and

his colleagues conducted a systematic review on 540 patients who were surgically treated for craniopharyngioma showed that the overall rate of new endocrinopathy for all patients undergoing surgical resection was 37% and Patients receiving GTR had over 2.5 times the rate of developing at least one endocrinopathy compared to patients receiving STR alone or STR + XRT. In this study, 22.5% of patients (9/40) have developed new endocrinopathies with overall post operative endocrinopathy is 90%. Pan hypopituitarism was identified in 25% of patients (10/40) which is higher than the report by Fernandez-Miranda, J. C et al's pathologic, clinical, and surgical review; He reported ten percent of patients are left with panhypopituitarism. (7). and DI was identified in 35% of patients (14/40). Pre operative DI has statistically significant positive association with post operative endocrinopathies (P-value<0.001)) and the size of the tumor has a statistically significant negative association with post operative endocrinopathies in multivariate regression analysis (P-value:0.046). The extent of resection has statistically strong association with the development of post operative DI (β: -0.346, t: -2.843, P-value: 0.007). In the review by Fernandez-Miranda, J. C et al., the visual outcomes were worse in patients receiving XRT after STR compared to GTR or STR alone (GTR = 3.5% vs. STR 2.1% vs. STR + XRT 6.4%, $P = 0.11$ but there is no statistically significant association between the visual outcome and extent of resection (P-value:0.625).

Regarding the surgical approaches, craniotomy and tumor resection and or ommaya insertion was done in 28 patients (70%) and microscopic/endoscopic TSS was done in 22.5% patients (9). Currently the endoscopic approach emerged as a credible surgical alternative to deal with suprasellar craniopharyngiomas and with advent of the techniques; almost all types of craniopharyngiomas can be a target for EEA. (4, 11). The major problem with this approach is CSF leak which is difficult to manage ones happen. (11). But in this study, there is no statistically significant difference between transcranial approach and transsphenoidal resection with respect to CSF leak. (P-value: 0.926). A meta-analysis comparing outcomes in children with craniopharyngioma treated with transsphenoidal surgery to those treated with conventional transcranial surgery reported that transcranial surgery was associated with increased rates of diabetes insipidus, postoperative worsening of vision, and postoperative nonvisual neurological deficits. (8). There is no statistically significant association between transsphenoidal and transcranial approach with post operative DI (P-value:0.11), post operative visual outcome (P-value: 0.403), post operative neurological outcome (0.827). A retrospective study on long-term

outcomes for surgically resected craniopharyngiomas by John M. Duff et al. showed that Tumors initially treated via transsphenoidal approaches were associated with good outcomes compared with transcranial approaches. (33). This is not reproduced in this study (P-value: 0.57). In general, as described by Fernandez-Miranda, J. C et al, whether transcranial or endonasal approaches are better suited for the treatment of suprasellar craniopharyngiomas may depend on lesion characteristics, patient characteristics, and surgeon's preference. (7) The timing and dose of radiotherapy after STR/biopsy is not well defined. 33 moon et al. compared the effect of early radiotherapy within 3 months of the initial surgery and the other group who received radiotherapy after progression or relapse and showed that overall survival and progression-free survival rates were similar, and visual acuity or field was better maintained, and DI was partly improved with early radiotherapy, but all deteriorated as the tumor progressed without early adjuvant radiotherapy. (35). In this study only 17.5% of patients (7/40) has received radiotherapy and all patients get the treatment after 3 months and difficult to compare early and late radiotherapy.

Duff et al. conducted a retrospective analysis of 121 patients to study the long-term outcome and showed that 60% of patients have good outcome. (33). Using his classification system based on Wen et al. functional independence measure, 67.5% (27/40) patients in this study have poor outcome and 32.5% (13/40) has good outcome. We found 23 patients (57.5%) were entirely dependent on others for self-care, 5 patients (12.5%) were partially dependent, 8 patients (20%) were independent and 4 patients (10%) were grossly normal and independent with Wen et al. functional independence measure. The factors that have statistically significant association with functional outcome on linear regression analysis includes post operative visual field (β-0.528, t-4.797, P-value<0.001), meningitis (β-0.288, t-2.897, P-value: 0.008), dysnatremia (β-0.278, t-2.749, P-value:0.011), and tumor size (β-0.227, t-2.124, P-value: 0.043). The association of functional outcome with post operative visual deterioration is also demonstrated by Diff et al. (33). The other factors described by Duff et al, like Lethargy at presentation, tumor calcification and hydrocephalus have no significant association with functional outcome in this study. Hypothalamic obesity is a feared complication especially in children and 40% of patients in Jörg Flitsch ' s study is suffering from obesity. (28). Forty-five percent of patents have developed post operative obesity which is in concert with the study by Kamaitachi et. al. Twenty-two patients (55%), had normal hypothalamic function based on CCSS, 11 patients (27.5%) have post op

obesity without behavioral change and 7 patients (17.5%) had obesity with hyperphagia. Patients who have sellar floor erosion on imaging have statistically significant negative association with hypothalamic function (β: -0.562, t: -4.806, P-value <0.001) in multiple linear regression analysis. Unexpectedly there is no association with Puget's grade of hypothalamic involvement with post operative hypothalamic function (P-value:0.76 in Pearson chi-square test).

Craniopharyngioma patients have decreased survival with an increased mortality rate by 3-6 folds higher than the general population and the overall 10-year survival rate ranges from 83%-93%. (36) Yaşargil et al. reported an intraoperative and early post operative mortality rate of 9.0% and the overall mortality rate was 16.7%. (37). The overall mortality rate in this study is 47.5% and brain abscess (β -0.293, t-2.63, P-value: 0.014), HCP (β-0.326, t-2.145, P-value: 0.041), hypothalamic involvement (β-0.479, t-3.148, P-value-0.004), dysnatremia (β- 0.299, t-2.586, P-value: 0.015) are the factors identified which are associated with significantly increased mortality. The mortality is much higher as compared to the report by Yasargil which may be due to the high infection rate in our institution and the challenge in the management of dysnatremia due to resource limitation (e.g., absence of hypertonic saline). Other important predictors of mortality in the literatures include female sex, childhood onset, hydrocephalus, tumor recurrence, body mass index and panhypopituitarism. This study doesn't show any significant association of mortality with sex (P-value: 0.7), Age (P-value-0.7), tumor recurrence (P- value: 0.308) and panhypopituitarism (p-value: 0.29).

The recurrence rate of patients in the study period was 5% (2/40). This is much lower than the report by Hyun Joo Park et al. which is 40% recurrence rate in his retrospective study of 64 patients. (38-41). In the literatures it is often quoted between 9-62%. (9.40). The factors associated with increased recurrence rate in the literatures include extent of resection, tumor biology, and adherence to critical neurovascular structures, hypothalamic involvement, and patient's age at presentation, lack of adjuvant radiation and duration of follow up. (9, 45-47). This study fails to prove the increased association of extent of resection (P-value:0.986), tumor pathology (P-value: 0.998), hypothalamic involvement (P-value:0.450), patients age at presentation (p-value: 0.998) and duration of follow-up (P-value: 0.067) with recurrence rate. This may be due to the small sample size and recurrence was assessed in only 16 patients

because in 24 patients the extent of resection was STR from the beginning and we can't assess recurrence in these group of patients.

7. Limitation of the study

The retrospective nature of the study design decreases the level of evidence driven from the results.

The sample size is small mainly due to the rarity of the pathology.

Since the study is multicenter, some of the radiologic findings are not consistently reported in a similar fashion and principal investigator fill this gap by interpreting the results according to the standards in the original literatures.

Since there is no standard institutional guideline for the management of patients with craniopharyngioma, the follow-up period was inconsistent but we took the mean follow up period to analyze the study.

8. Conclusions and Recommendations

Craniopharyngioma is associated with very high rate of mortality rate in our setup and higher grade of hypothalamic involvement and signs of increased ICP at presentation are predictors of mortality. Majority of the survivors have also significant ophthalmologic, neurologic and endocrinologic morbidities.

More than two third of the patients have poor functional outcome which is higher as compared to other studies and aggressive treatment of meningitis and dysnatremia with better ICU care may improve the overall outcome of these patients.

The larger tumor size is also associated with poor functional outcome; early referral to tertiary centers for imaging for earlier detection and more frequent follow-up imaging and intervention may improve overall outcome.

The majority of our patients receive STR which seems rational since most patients have higher grade hypothalamic involvement which is also associated with higher mortality rate. Hypothalamic obesity is also a major complication in these patients.

GH is the most common hormonal deficiency in patients with craniopharyngioma in most literatures but in our set-up, it is not determined in more than two-third of the cases mainly due to financial constraint to do IGF-1. At least we can determine baseline GH and to have follow-up comparison.

Although STR was done in more than half of the patients, radiotherapy was offered in only 29% of patients which is the major obstacle in the management of patients with craniopharyngioma. Establishment of more radiotherapy centers is warranted due to huge waiting list of patients for radiotherapy. There should be a collaboration from the Hospital to the ministry of health at national level for this work

Finally, we recommend to conduct a prospective study to better understand the causal relationships of long-term complications with the mortality that occur out of the hospital; these are poorly documented in this retrospective study.

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9. Annexes

I: Questionnaire

I: Sociodemographic Data

1. Age/Sex
2. MRN
3. Phone No

II. Clinical Assessment

1. Headache 1) yes 2) no
2. Vomiting 1) Yes 2) no
3. Nausea 1) Yes 2) No
4. Visual deterioration 1) Yes 2) No
5. Lethargy 1) yes 2) No
6. Short stature 1) Yes 2) No
7. Failure of sexual development 1) Yes 2) No
8. Obesity 1) Yes 2) No
9. Polyuria/polydipsia 1) Yes 2) No
10. Seizure 1) Yes 2) No

11. BMI; 1) <18.5 2) 18.5-24.9 3) 25-29.9 4) >30
12. Bitemporal hemianopsia 1) Yes 2) No
13. Junctional Scotoma 1) Yes 2) No
14. Hemianopsia 1) Yes 2) No
15. Quadrantanopsia 1) Yes 2) No
16. Visual acuity:
    a. Rt: 1) NLP 2) LP 3) HM 4) Close range 5) 3m 6) 6m
    b. Lt: 1) NLP 2) LP 3) HM 4) Close range 5) 3m 6) 6m
17. Visual filed: 1) cut present 2) cut absent
18. If cut present; 1) uni temporal 2) Bitemporal 3) nasal
19. Other CN deficit: 1) yes 2) No
20. If CN deficit: 1) CN-3 2) CN-4 3) CN-5 4) CN-6
21. Optic atrophy: 1) Present 2) Absent
22. If Optic atrophy present: 1) Unilateral 2) Bilateral
23. Papilledema: 1) Present 2) Absent
24. Hemiparesis: 1) Present 2) Absent

III. Pre op endocrine dysfunction

25. GH deficiency; 1) yes 2) No 3) status Unknown
26. Thyroxine deficiency; 1)yes 2) No 3) Status Unknown
27. Cortisol deficiency; 1) Yes 2) No 3) Status unknown
28. Sex hormone deficiency; 1) yes 2) No 3) status Unknown
29. PRL: 1) Normal 2) Low 3) High
30. DI; 1) present 2) absent

Pre op imaging features

31. Tumor size; 1) <3cm 2) 3-6 cm 3)> 6cm
32. Enhancement: 1) Yes 2) No
33. Cystic component: 1) Yes 2) No
34. Calcification: 1) Yes 2) No
35. Mass effect: 1) Yes 2) No
36. Sellar enlargement: 1) Yes 2) No

37. Major suprasellar component: 1) Yes 2) No
38. Optic Nerve involvement: 1) Yes 2) No
39. Subfrontal extension; 1) Yes 2) No
40. HCP: 1) Yes 2) No
41. If yes mode of intervention: 1) Shunt 2) ETV 3) Definitive surgery
42. Third ventricular involvement; 1) Yes 2) No
43. Hypothalamus; Puget grade- (1) Grade 0 2) Grade 1 3) Grade 2
44. Middle fossa involvement; 1) Yes 2) No
45. Posterior fossa involvement; 1) Yes 2) No
46. Hemorrhage: 1) Yes 2) No
47. Vascular encasement: 1) Yes 2) No
48. If yes; which vessel? 1) ICA 2) Basilar 3) MCA 4) ACA
49. Treatment; 1) surgery 2) radiation therapy 3) both 4)chemotherapy 5) observation 6) ETV 7) shunt
50. If surgery, type of surgery; 1) craniotomy 2) TSS 3) Omaya insertion
51. Surgical Approach: 1) Pterional 2) Subfrontal 3) Combined
52. Extent of resection; 1) GTR 2) STR 3) Biopsy
53. If STR why; adherent to-1) neurovascular structures 2) Pituitary stalk 3) Optic Chiasm 4) Hypothalamus 5) reason not mentioned
54. Histopathology: 1) Adamantinomatous 2) Papillary

Post op course and complications

55. Length of hospital stay: 1) 1wk 2) 2 wks 3) 4wks
56. Tracheostomy: 1) yes 2) No
57. CSF leak : 1) Present 2) absent
58. Meningitis: 1) Yes 2) No
59. Brain Abscess: 1) Yes 2) No
60. Other HAI: 1) Yes 2) No
61. Pneumocephalus: 1) Yes 2) No
62. HCP: 1) Yes 2) No

63. Intracranial Hematoma:1) Yes 2) No
64. Vasospasm: 1) Yes 2) No
65. Vascular Injury: 1) Yes 2) No
66. Ophtalmologic Evaluation
    a. Visual Acuity;
        a. Rt: 1) improved 2) worsened 3)same
        b. Lt: 1) improved 2) worsened 3)same
    b. Visual Field;
        a. Rt: 1) improved 2) worsened 3) same
        b. Lt: 1) improved 2) worsened 3)same
67. Endocrinopathies: 1) No 2) Panhypopituitarism 3) Hypocortisolism 4) Hypothyroidism 5) Hypogonadism 6)Hyper prolactinomas 7) DI 8) combined
68. Recurrence: 1) yes 2) No
69. No of recurrence: 1) 1 2) 2 3) 3
70. Treatment for recurrence: 1) surgery 2) radiotherapy 3) both 4) Observation
71. Craniopharyngioma Clinical Status Scale (CCSS)

I. CCSS: Neurological

1. No deficiet/Seizure
2. Mild deficit (CN palsy, Seizure well controlled)
3. Moderate deficit (mild hemiparesis,independent ambulation, moderately controlled seizure)
4. Sever deficit(moderate to sever hemiparesis, major stroke, lethargy or abulia)

II. CCSS: Visual

1. Normal VA and VFs
2. Mild acuity deficit/field cut
3. Unilateral blindness/homonymous hemianopia/bilateral hemianopia
4. Bilateral blindness/nearly functional blindness

III. CCSS: Pituitary

1. Normal anterior and posterior pituitary function
2. mild anterior pituitary dysfunction(1 or 2 hormone supplement)
3. DI with or without mild anterior pituitary dysfunction(1 or 2 hormone replacement)
4. DI and panhypopituitarism

IV. CCSS: Hypothalamic

1. Normal Hypothalamic function
2. Post op Obesity (BMI>2SD), no beharioural or psychological Sxs
3. Obesity (BMI>2sd) + Hyperphagia or BMI>3SD-Hyperphagia
4. Extreme obesity (BMI>4SD) and Hyperphagia, behavioural disturbance, problems of sllep wake cycle, memeory

V. CCSS: Educational

1. Excellent acadamic performance/occupational success
2. good academic performance at grade level/maintaining employment
3. Behind in grade academically, needs tutor, dont maintain persistant employment
4. Completely dependent on others for self care/sever cognitive deficit

72. Functional Classification scale

1. Grossly normal and independent/mild hormonal disturbance/seizure controlled with meds
2. Independent; panhypopituitarism, mild to moderate visual compromise,CN deficit, mild psychological dysfunction
3. Partially dependent; serious visualcompromise, serious neurologic deficit(hemiparesis and refractory seizure)
4. Entirely dependent on others for self care