Endocrinological Outcome Among Treated Craniopharyngioma Patients

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Introduction

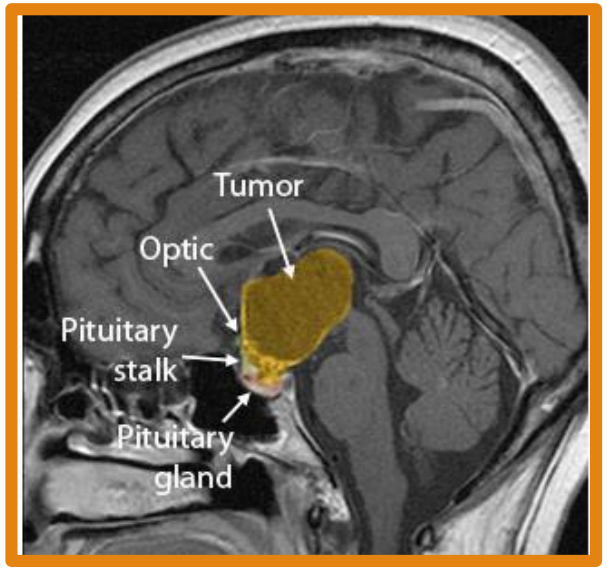
Craniopharyngiomas are benign neoplastic lesions which are presumed to originate from the embryological remnants of Rathke's pouch.

They may be located in the suprasellar region, within the sella or both and because of infiltration of surrounding structures they may have extensive adverse consequences

They account for 5-10% of intracranial tumors in

children

Peak incidence is in the first decade



Endocrine abnormalities

Caused by direct damage to or compression of normal structures can lead to a range of endocrine abnormalities

Deficiency of fallowing hormones

- Growth hormone
- Gonadotropin (FSH,LH)
- TSH
- ACTH
- Diabetes insipidus is frequent when the pituitary stalk is involved

Growth failure is the most common presentation of hormonal deficiency

Hormone deficiency	Presentation	Symptoms and signs
Adrenocorticotrophic hormone	Acute	Fatigue, weakness, dizziness, nausea, vomiting, circulatory failure. As in Addison's disease, except lack of hyperpigmentation, absence of hyperkalaemia
	Chronic	Tiredness, pallor, anorexia, nausea, weight loss, myalgia, hypoglycaemia
Gonadotrophins	Children	Delayed puberty
	Men	Impaired fertility, impotence, reduced libido, decreased muscle mass and strength, decreased bone mass, decreased erythropoiesis and hair growth, fine wrinkles, testicular hypotrophy
	Women	Amenorrhoea, oligomenorrhoea, infertility, loss of libido, dyspareunia, fine wrinkles, breast atrophy, osteoporosis, premature, atherosclerosis
Thyroid-stimulating hormone	Children	Growth retardation
	Adult	Fatigue, cold intolerance, constipation, weight gain, dry skin, slow relaxing reflexes
Growth hormone	Children	Growth retardation, short stature, increased adiposity
	Adult	Reduced exercise capacity, impaired psychological wellbeing, increased cardiovascular risk, increased central obesity, reduced lean body mass
Prolactin		Failure of lactation
Antidiuretic Hormone		Polyuria, polydipsia including nocturnal

Baseline assessment of endocrine function

- Endocrine function should be assessed and significant abnormalities corrected prior to surgery if possible
  - ACTH,Cortisol (0900)
  - Free T4, TSH
  - serum and urine osmolality , electrolyte
  - Insulin-like growth factor
  - Testosterone, estradiol, LH, FSH
  - Prolactin

Postoperative evaluation

- Endocrine function should be assessed
  - Serum ,ACTH,Cortisol (0900)
  - Free T4, TSH
  - serum and urine osmolality , electrolyte
  - Insulin-like growth factor (assess GH) → GH stimulation test
  - Testosterone, estradiol, LH, FSH
  - Prolactin

Endocrine evaluation

To test basal ACTH secretion, serum cortisol should be measured at 8 to 9 AM, and the results should be interpreted as follows:

normal range 5 to 25 mcg/dL (138 to 690 nmol/L)

- Cortisol value of ≤3 mcg/dL (83 nmol/L) is abnormal
- Cortisol value of ≥18 mcg/dL (497 nmol/L) is excellent
- Cortisol value >3 mcg/dL (83 nmol/L) but <18 mcg/dL (497nmol/L)

  that is persistent on repeat (need ACTH stimulation test)

Endocrine evaluation

Asses ACTH reserve

- Metyrapone test
- Insulin-induced hypoglycemia test
- ACTH (Cosyntropin stimulation test)

KFSHRC experience

J Pediatr Endocrinol Metab. 2001 Jul-Aug;14(7):869-74.

Endocrine sequelae of childhood craniopharyngioma.

Bin-Abbas B[1], Mawlawi H, Sakati N, Khafaja Y, Chaudhary MA, Al-Ashwal A.

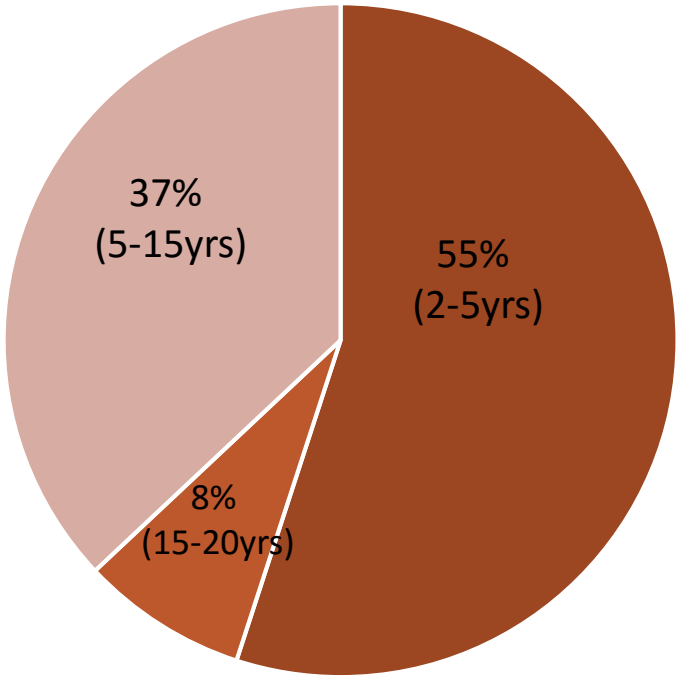
- The endocrine sequelae of 62 children with craniopharyngioma were studied retrospectively.
- Complete surgical resection was achieved in 30 patients and 32 patients had residual tumor
  Twenty-five patients had recurrence or progression of the residual tumor and were treated with radiotherapy
- The most common presenting symptoms were headache, nausea and vomiting, followed by growth failure
- Pre-operatively, GHD was the most commonly encountered pituitary hormonal deficiency
- Postoperatively, most children had diabetes insipidus
- Multiple pituitary hormonal deficiencies were more frequently observed in children treated with extensive radical surgery than in those treated with conservative surgery and radiotherapy
- The endocrine morbidity associated with craniopharyngioma and its different management modalities remains high; however, it is manageable with appropriate hormonal replacement therapy.

KFSHRC experience (2001-2012)

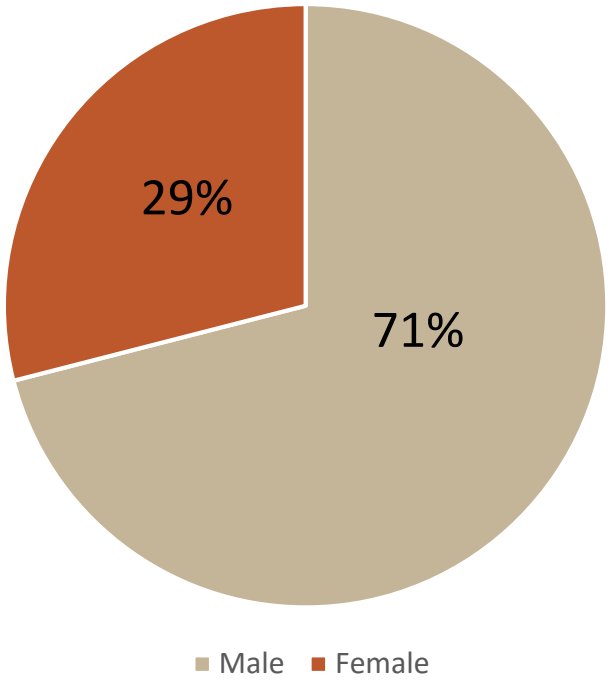
- The endocrine sequelae of 38 children with craniopharyngioma were studied retrospectively initially operated on from 2001– 2012
  - 31 patient had total surgical resection
  - 7 patient had subtotal surgical resection
  - 6 patient had recurrence
  - Total of 11 patient required radiation therapy
- Fallowed up 4-14 years (mean: 8 years)
- The most common presenting symptoms were headache, visual impairment

Age at diagnosis

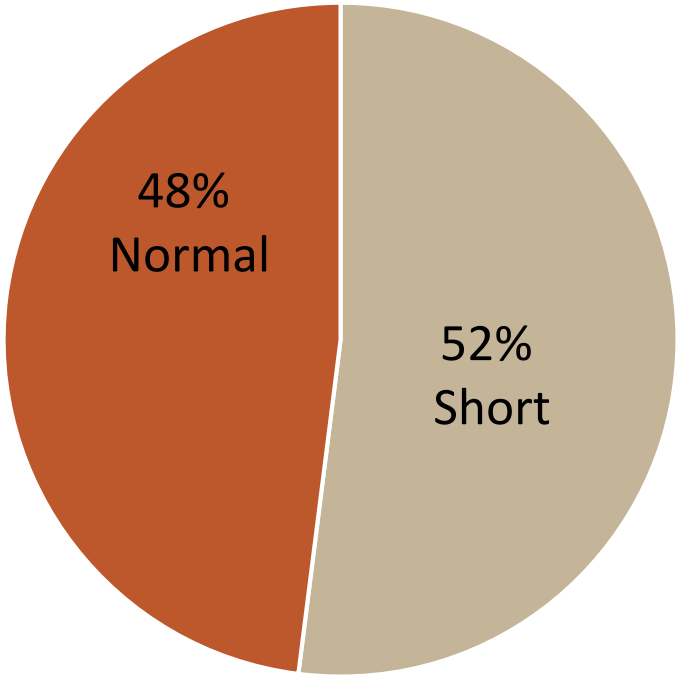
- Age at diagnosis range (2-19 years), mean 7.5 years
- 55% < than 6 years



- Majority were males
  - 11 female
  - 27 male

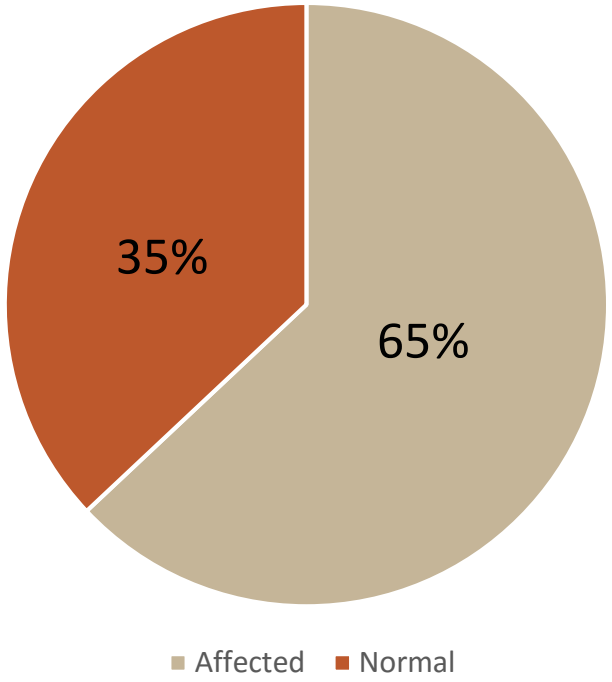


20 Patient had short stature at presentation

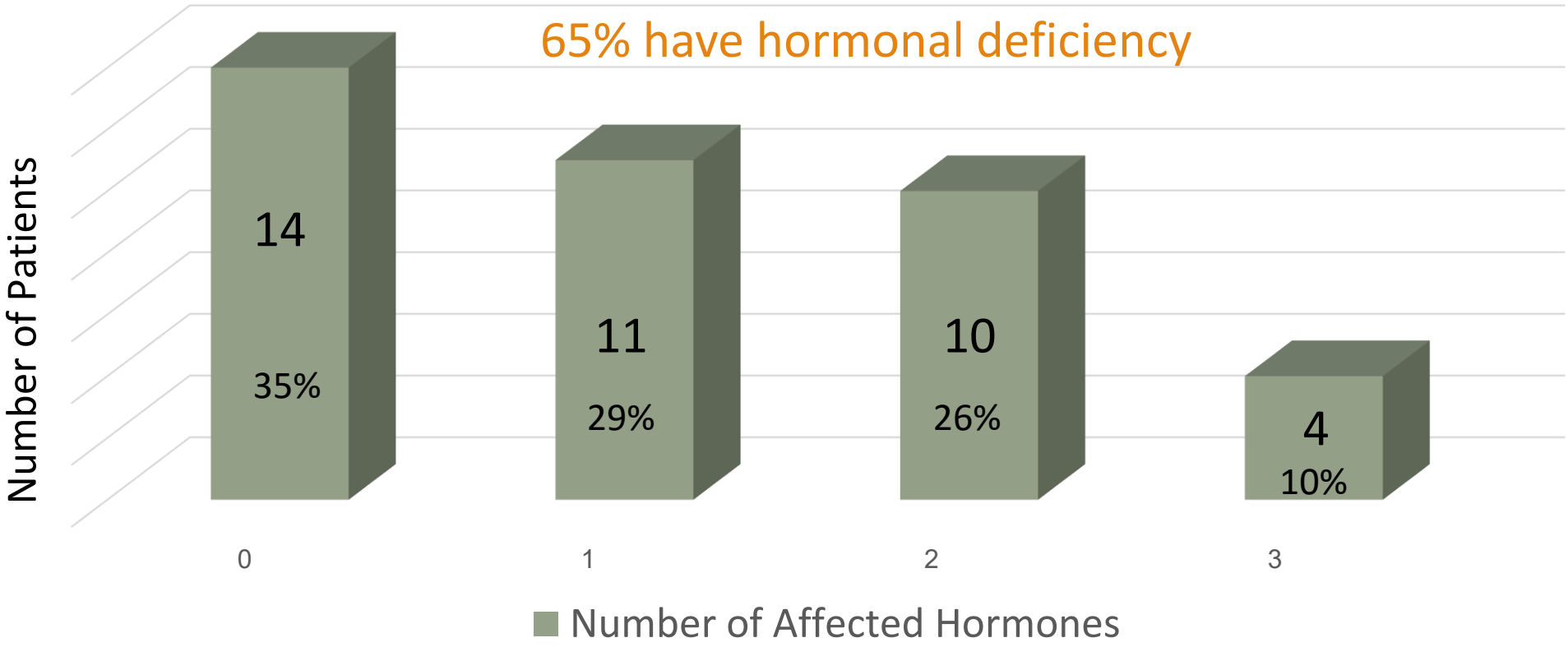


Preparative Hormonal Deficiency

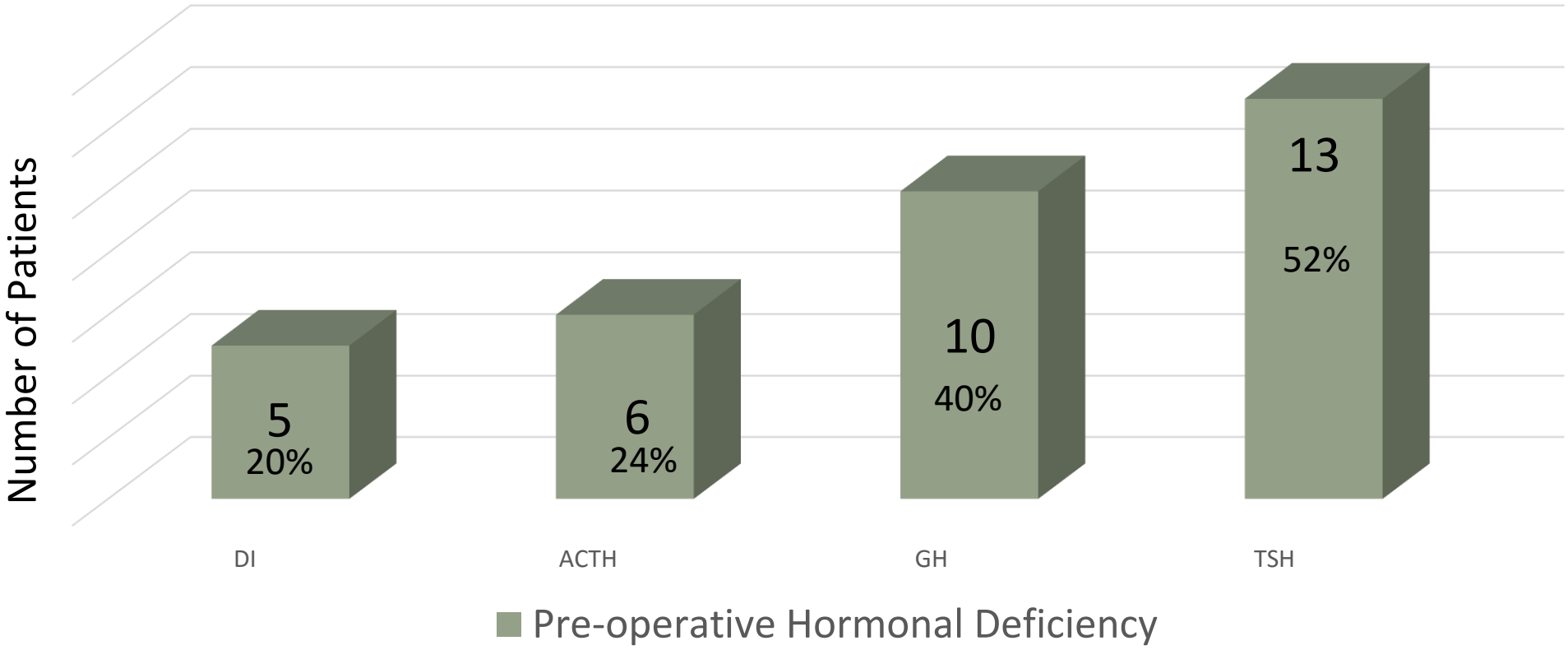
65% of patients had at least 1 hormonal abnormality at diagnosis



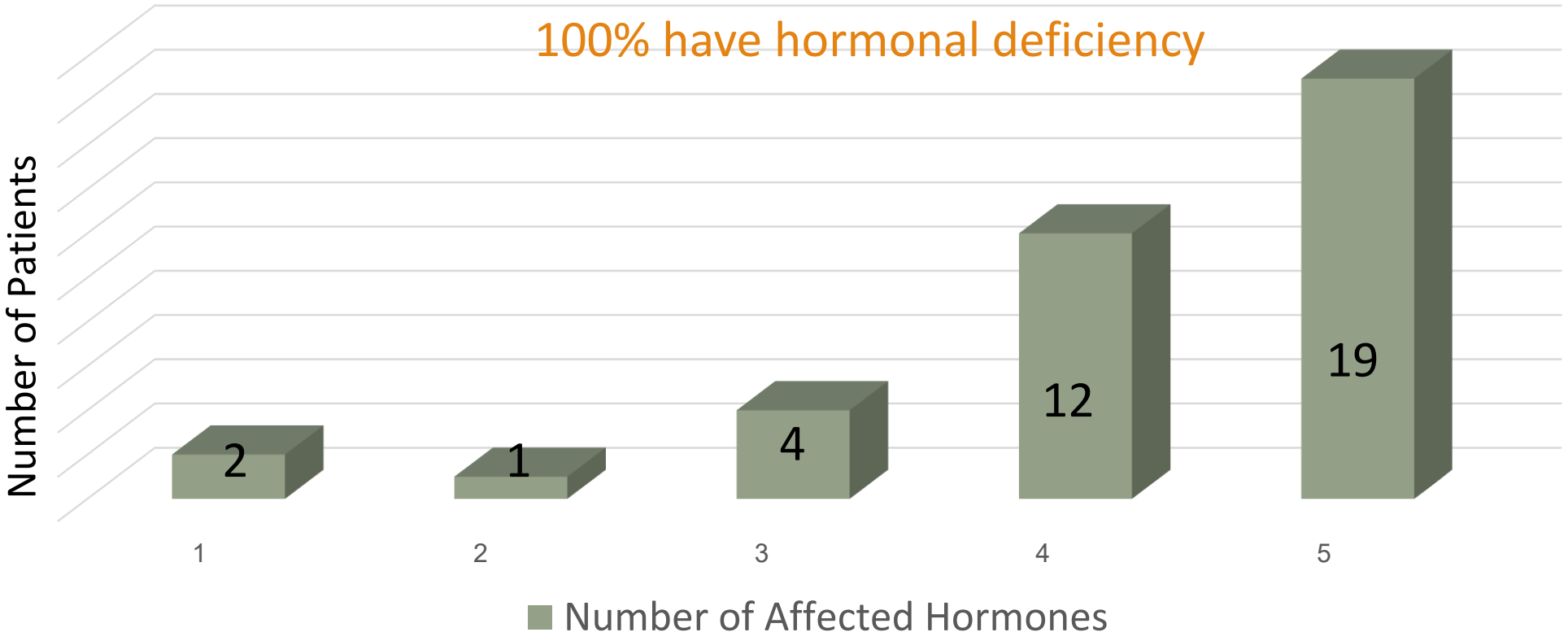
Pre-operative Hormonal Deficiency



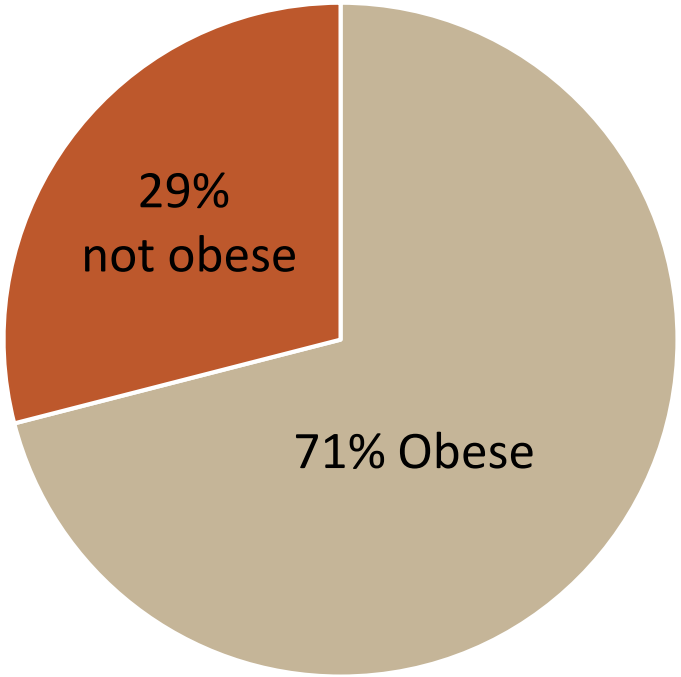
Pre-operative Hormonal Deficiency



Post-operative Hormonal Deficiency



27 Developed Obesity



Conclusions

- 38 children, were evaluated. The mean follow-up period was 8 years
- The most common symptoms were headache, nausea and vomiting and visual impairment
- Preoperative presentation 20% were short , 65% had at least one hormonal deficiency the commonest was hypothyroidism
- After tumor treatment, multiple pituitary hormonal deficiencies happened, and required hormonal replacement therapy(in GTR and STR) no difference between the 2 groups 80% had more than 4 hormones deficiency .
- All patient above age of 15 had hypogonadism
- 5 children grew normally without GH despite GHD
- Obesity was frequent postoperative 71% of patients

J Pediatr. 1980 Nov;97(5):728-35.

Endocrine and neurologic outcome in childhood craniopharyngioma: Review of effect of treatment in 42 patients.

Thomsett MJ, Conte FA, Kaplan SL, Grumbach MM.

- Forty-two cases of craniopharyngioma in children reviewed
- Only 9.5% had sought medical attention because of symptoms suggesting hormonal deficit
- Growth retardation was present in 53% and growth hormone deficiency was documented in 72% before treatment
- Multiple hypothalamic-pituitary hormone deficiencies were present in all patients after treatment

Pediatric Research (1993) 33, S29–S29; doi:10.1203/00006450-199305001-00156

ENDOCRINE OUTCOME OF SURGICAL REMOVAL OF CRANIOPHARYNGIOMAS

J Curtis[1], R M Ehrlich[1], D Daneman[1] and H Hoffman[1]

[1]Dept. Pediatrics & Neurosurgery, U of Toronto and The Hospital For Sick Children, Toronto, Canada M5G 1X8

- They reviewed the endocrine outcome of 34 cases (23 boys, 17 girls mean age 8.8 yrs) of craniopharyngioma initially operated on from 1980-89
- Adrenal insufficiency 89%
- Hypothyroidism 96%
- hypogonadism 100%
- Diabetes insipidus occurred in 32, permanent
- 24% were below the 3rd % preoprative
- 16 cases became obese

Conclusions Following attempted total removal of C almost all were hypopit, half became obese and most obese patients did not require GH

J Pediatr Endocrinol Metab. 2006 Apr;19 Suppl 1:431-7.

Endocrine and growth features in childhood craniopharyngioma: a mono-institutional study.

Di Battista E[1], Naselli A, Queirolo S, Gallarotti F, Garré ML, Milanaccio C, Cama A.

- 32 children, 18 males and 14 females, were evaluated. The mean follow-up period was 6.3
- The most common symptoms were headache, nausea and vomiting, visual impairment, and neurological changes
- Preoperative presentation(five polyuria and polydipsia, five growth failure, two precocious puberty, eight obesity or overweight)
- After tumor treatment, multiple pituitary hormonal deficiencies, especially growth hormone (GH) deficit (GHD) were found and required hormonal replacement therapy
- Eight children grew normally without GH despite GHD
- Obesity was frequent and was often associated with hyperinsulinism and hyperphagia.

J Neurooncol. 2011 Feb; 101(3): 463–476.
Published online 2010 Jun 10. doi: 10.1007/s11060-010-0265-y
PMCID: PMC3024496

Endocrinologic, neurologic, and visual morbidity after treatment for craniopharyngioma

Michael E. Sughrue,[1] Isaac Yang,[1] Ari J. Kane,[1] Shanna Fang,[1] Aaron J. Clark,[1] Derrick Aranda,[1] Igor J. Barani,[2] and Andrew T. Parsa[1]

Summary of various types of monohormonal and polyhormonal endocrinopathy following treatment of craniopharyngioma 540 Patient, GTR still increased the rate of post-operative endocrinopathy by over three fold

	GTR (%)	STR (%)	STR + XRT (%)	fXRT	SRS (%)
Hyperprolactinemia	0.0	0.0	0.9	N/A	0.0
Hypogonadism	3.5	2.1	1.8	N/A	3.0
Hypothyroid	13.8	5.7	1.8	N/A	7.6
GH deficiency	6.2	1.4	1.8	N/A	0.0
ACTH deficiency	14.5	6.4	0.9	N/A	3.0
Anterior panhypopituitarism	11.8	3.5	10.0	N/A	3.0
DI	18.7	6.4	5.5	N/A	0.0
Obesity	2.1	0.7	2.7	N/A	1.5
Any endocrinopathy	51.9	19.9	20.0	N/A	18.2

Childs Nerv Syst. 2013 Feb;29(2):231-8. doi: 10.1007/s00381-012-1926-2. Epub 2012 Oct 23.

A systematic review of the results of surgery and radiotherapy on tumor control for pediatric craniopharyngioma.

Clark AJ[1], Cage TA, Aranda D, Parsa AT, Sun PP, Auguste KI, Gupta N.

A total of 109 studies described extent of resection resulting in a cohort of 531 patients

Although there are limitations of a systematic review of retrospective data, ther esult suggest that STR+XRT of pediatric craniopharyngioma is associated with similar rates of tumor control as GTR

Hormonal replacement therapy

- GH started (0.02- 0.03) mcg/kg OD
- Hydrocortisone started as soon as possible 8-12mg/m2
- Levothyroxine started after H-C or at the same time to maintain FT4 in the higher normal range, at a dosage of 1.5-2 mcg/kg OD
- Minirin (DDAVP) was started as soon as possible, elicited no symptoms, and maintained normal electrolyte levels (0.1-0.2 mg/m2)
- Sex steroid to be stared after 13 years in girls and 14 years in boys (no puberty)

Growth hormone treatment and risk of recurrence or development of secondary neoplasms in survivors of pediatric brain tumors ??

J Clin Neurosci. 2014 Dec;21(12):2155-9. doi: 10.1016/j.jocn.2014.04.016. Epub 2014 Jul 22.

Growth hormone treatment and risk of recurrence or development of secondary neoplasms in survivors of pediatric brain tumors.

Wang ZF[1], Chen HL[2].

This meta-analysis assessed whether GH treatment was associated with risk of recurrence or development of secondary neoplasm for brain tumors in children

No evidence that GH therapy is associated with an increased risk of recurrence for pediatric brain tumors. However, because of our small sample size, the association of GH therapy with an increased risk of secondary neoplasm is uncertain. Further prospective cohorts are needed.

The endocrine morbidity associated with craniopharyngioma and its different management modalities remains high however, it is manageable with appropriate hormonal replacement therapy

1st PAPNS Conference & ISPN Course

Pan Arab Pediatric Neurosurgery Society

Thank you for attention.