Table 1: Investigations undertaken and their performance

	Abnormal N (%)	Median (range)	Interpretation of test
Urinary Free Cortisol (nmol/24h)	17/18 (**94**)	1126 (41-30287)	Abnormal: >275nmol/24h
Midnight$^{\varphi}$ cortisol (nmol/l)	27/27 (**100**)	555 (169-2987)	Abnormal: >138nmol/l
8am cortisol (nmol/L)	10/27 (37)	601 (95-2990)	Abnormal: >550nmol/l
8am ACTH (ng/l): **- Pituitary tumours** **- Adrenal tumours** **- Ectopic ACTH**	 11/12 (92) 8/10 (80) 1/2 (50)	 46 (2.5-66) 4 (2.5-71) 46 (40-52)	 >15ng/l: ACTH-dependent <5ng/l: ACTH-independent 3-15ng/l: ACTH-dependent or independent
LDDST +48h: cortisol (nmol/l) ***(20mcg/kg/day 6hrly)***	20/20 (**100**)	588 (74-1355)	Suppression means cortisol at +48h <50nmol/l
HDDST +48h: ***(80mcg/kg/day 6hrly)*** **- Pituitary tumours** **- Adrenal tumours** **- Ectopic ACTH**	Failure of suppression: 1/10 (10) 6/6 (**100**) 1/2 (50)		Suppression means cortisol at +48h <50% of basal value
CRH test ***(100mcg)*** **- Pituitary tumours** **- Adrenal tumours** **- Ectopic tumour**	Rise in ACTH or Cortisol 8/9 (89) 0/1 (0) 1/2 (50)		Response if: cortisol ↑ >20% ± ACTH ↑ >50%
IPSS with CRH: **- Pituitary tumours** **- Adrenal tumours** **- Ectopic tumour**	 5/5 (**100**) -- 1/1 (**100**)		•Lateralisation: interpetrosal ratio of ACTH after CRH >1.4 •Central-to-peripheral ACTH gradient > 2 before, and > 3 after CRH administration indicative of Cushing disease

In the second column, the numerator indicates the number of abnormal test result; the denominator indicates the number of subjects in whom the test result was available.

N: Number of patients. %: Percentage. ACTH: Adrenocorticotropic hormone. LDDST: Low dose dexamethasone suppression test. HDDST: High dose dexamethasone suppression test. CRH: Corticotropin releasing hormone. IPSS: Bilateral inferior petrosal sinus sampling

$^{\varphi}$ Sleeping value

Table 2: Clinical Presentation and type of treatment administered

		ALL Cushing syndrome patients [N:30]	Pituitary Cushing Disease [N:16]	Adrenal Cushing [N:11]	Ectopic Cushing [N:2]	Unknown etiology [N:1]
CLINICAL PRESENTATION						
Years [Median (range)]	**Age at presentation**	8.9 (0.2-15.5)	10 (7-15.5)	1.5 (0.2-10.2)	6.7 (2.0-11.4)	7.0
	Time lapse between 1st signs and diagnosis	1.0 (0.04 – 6.0)	1.5 (0.1 – 6.0)	0.5 (0.1-3.2)	0.7 (0.04-1.5)	1.0
Number of cases (%)	**Weight gain**	**23 (76.6%)**	**15 (94%)**	**5 (45.4%)**	2 (100%)	1 (100%)
	Hirsutism	**17 (56.6%)**	6 (37.6%)	**8 (72.7%)**	2 (100%)	1 (100%)
	Acne	15 (50%)	8 (50%)	**5 (45.4%)**	2 (100%)	0 (0%)
	Hypertension	15 (50%)	8 (50%)	4 (36.4%)	2 (100%)	1 (100%)
	Mental changes/poor school performance	13 (43.33%)	7 (43.7%)	4 (36.4%)	2 (100%)	0 (0%)
	Fatigue or weakness	12 (40%)	6 (37.5%)	4 (36.4%)	2 (100%)	0 (0%)
	Growth retardation	11 (36.6%)	**10 (62.5%)**	1 (0.9%)	0 (0%)	0 (0%)
	Striae	8 (26.6%)	7 (43.7%)	0 (0%)	0 (0%)	1 (100%)
	Secondary sexual development	Early: 8 (26.6%) Delayed: 3 (10%) Normal: 19 (63.3%)	Early: 5 (31.2%) Delayed:3(18.7%) Normal: 8 (50%)	Early:2(18.2%) Delayed:0(0%) Normal: 9(82%)	Early:1(50%) Delayed: 0 Normal: 1(50%)	Early:0(0%) Delayed:0(0%) Normal: 1(100%)
	Easy bruising	6 (20%)	3 (18.7%)	2 (18.2%)	1 (50%)	0 (0%)
	Sleep disturbances	6 (20%)	3 (18.7%)	2 (18.2%)	0 (0%)	1 (100%)
	Hypokalemia	4 (13.3%)	1 (6.2%)	3 (27.3%)	0 (0%)	0 (0%)
	Hyperpigmentation	2 (6.6%)	2 (12.5%)	0 (0%)	0 (0%)	0 (0%)
TYPE OF TREATMENT						
Number of cases	**Surgery only**	14	9	5	0	0
	Surgery + Antihypertensive agent/s	3	1	2	0	*
	Surgery + Radiotherapy	3	3 (+ metyrapone in 1 case); (+ bilateral adrenalectomy in 1 case)	0	0	0
	Surgery + Metyrapone	3	1	1	1	0
	Surgery + Antihypertensive agent/s + Metyrapone	4	2	2	0	0
	Surgery + Chemotherapy	2	0	1	1 (+ phase I HIPEC$^{\varphi}$ trial)	0

N: Number of patients. 1st: First *Managed with antihypertensive agents whilst investigations and surgery deferred. Lost to follow up in our centre.

φHIPEC: Hyperthermic Intra-Peritoneal Chemotherapy

Table 3. Auxology on follow-up of the whole cohort

	Diagnosis (n=30)	6 Months (n=17)	1 Year (n=14)	2 Years (n=12)	End of growth (n=4)
Median height (SDS (range))	-0.3 (-3.2 to 3.0)	-0.5 (-5.0 to 0.4)	-0.1 (-3.5 to 1.1)	0.0 (-3.4 to 1.3)	-0.5 (-3.1 to 0.4)
Median weight (SDS (range))	+1.7 (-2.8 to 4.0)	0.9 (-3.7 to 3.0)	0.6 (-4.0 to 3.8)	1.1 (-2.4 to 4.5)	1.0 (0 to 2.1)
Median BMI (SDS (range))	2.1 (-6.5 to 4.6)	1.4 (-1.0 to 3.5)	0.5 (-2.5 to 3.7)	1.1 (-1.0 to +3.9)	1.3 (0 to +2.9)
Number of cases (%) with BMI > 2 SDS	14 (46%)	6 (35%)	4 (28%)	3 (25%)	1 (25%)
Median growth velocity (SDS (range))			0.6 (-3.7 to 3.8)		
Number of cases (%) with hypertension	15 (50%)		4 (28%)		

n: Number of patients. SDS: Standard Deviation Score.

.

Table 4. Post-treatment endocrine and non-endocrine complications

	Cushing Disease [N:16]	Adrenal hypercortisolism [N:11]	Ectopic hypercortisolism [N:2]
HORMONAL COMPLICATIONS			
ACTH deficiency (long term)	6	-	-
Transient Diabetes Insipidus	11	-	-
Persistent Diabetes Insipidus	2	-	-
Childhood GH deficiency	7	-	-
TSH deficiency	3	-	-
Gonadotropin deficiency	2*	-	-
Panhypopituitarism (≥4 deficiencies)	1	-	-
Insulin insensitivity	1	-	-
Primary mineralocorticoid deficiency	-	3	-
Primary glucocorticoid deficiency (long term)	-	7	-
Cortisol suppression (long term)	-	-	1
ENDOCRINE UNRELATED COMPLICATIONS			
Relapse	3	1	1
Incomplete resection	3	-	1
Second neoplasia	-	1	-

Death	-	1	-
Deep vein thrombosis	1	-	-
Septic shock	-	1	-
Cerebrospinal fluid leak	1	-	-
Chylous effusion	-	-	1

CS: Cushing syndrome. CD: Cushing disease. ACTH: Adrenocorticotropic hormone. GH: Growth hormone. TSH: Thyroid stimulating hormone

*Out of all the 16 cases of CD; all of them old enough to have gone through puberty.