

# How useful is 24 hour Urinary Free Cortisol as a Screening Tool for Cushing's syndrome?

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## Introduction:

Cushing's syndrome (CS) is a rare disease that can be difficult to diagnose. 24 hour urinary free cortisol (UFC) is one of the reliable screening tests to diagnose CS. The Endocrine Society recommends against widespread screening for CS. It advises to screen those patients presenting with multiple and progressive features (easy bruising, facial plethora, proximal myopathy and striae) of CS., in addition to patients who experience unusual features for their age (osteoporosis, hypertension).

## Methods:

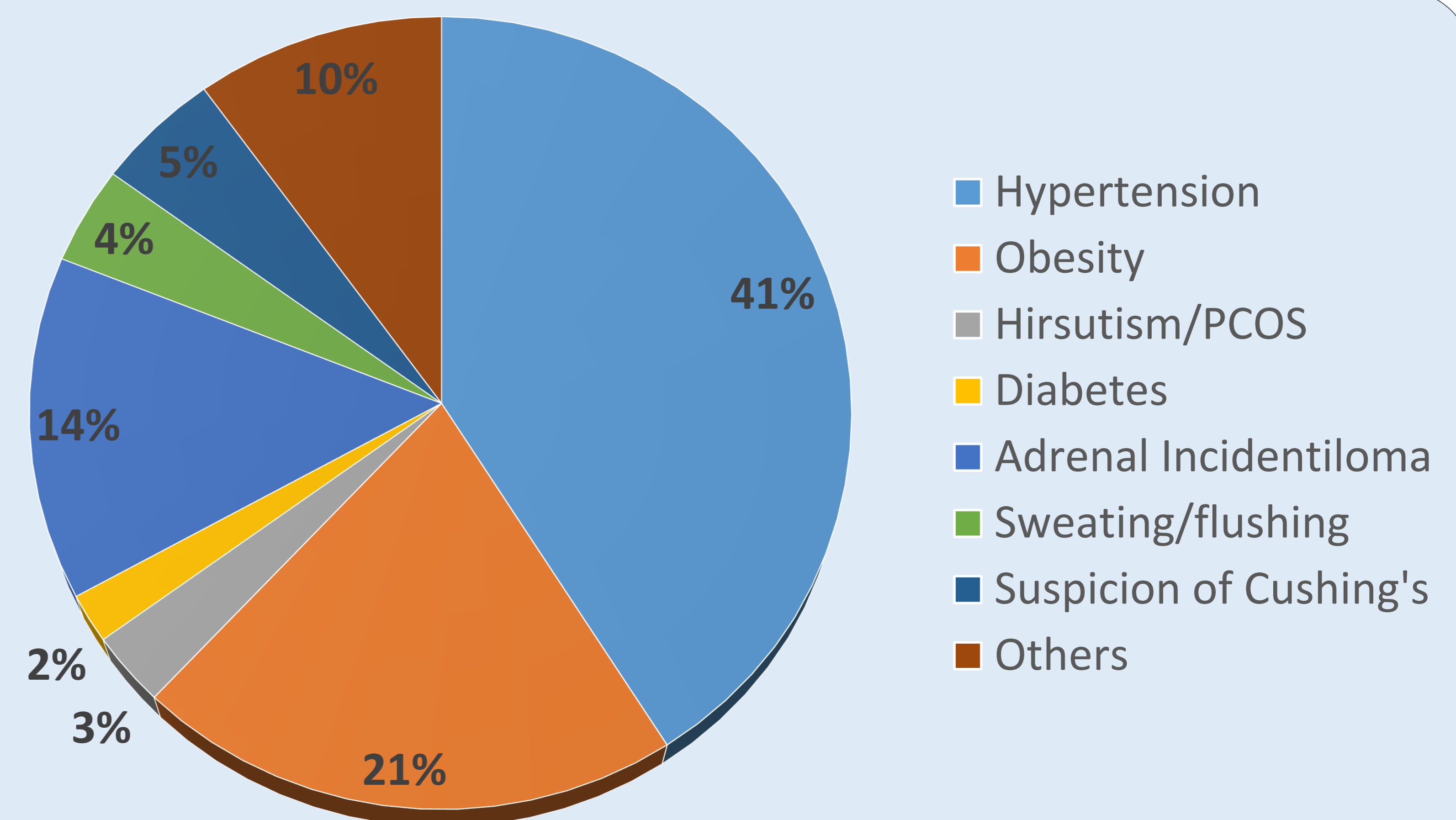
- A retrospective audit was done to assess our practice of requesting 24hour UFC in patients attending diabetes, endocrine and weight management clinics in Mid-Yorkshire Hospitals over 3 years (2014-2016). During this period, 649 samples (507 patients) of 24h UFC were recorded. Patients already diagnosed with CS and patients with insufficient clinical information were excluded.
- The medical records of included patients were reviewed for: age; gender; body mass index (BMI) in kg/m<sup>2</sup>; phenotype (normal or Cushingoid - defined by presence of stria rubra, easy bruising, facial plethora and/or proximal myopathy); presence or absence of diabetes; presence or absence of hypertension.
- 24h urinary free cortisol is analysed using liquid chromatography- mass spectrometry (LC-MS/MS), with 24h UFC titer more than 147 nmol considered positive.
- Final diagnosis of Cushing's syndrome was based on consultant diagnosis after conducting all necessary confirmatory tests.

## Results:

356 patients were eligible for final analysis. 66.4% of the patients were females. The mean age in our cohort was 44.9 years (SD 16.7 years) and the mean BMI was 35.8Kg/m<sup>2</sup> (SD 9.18 kg/m<sup>2</sup>). 61% of the patients had hypertension and 21.6% had diabetes. The reasons for requesting 24h UFC is summarized in **figure 1**.

A chi-squared test for association conducted on all patients with recorded BMI revealed no evidence that BMI category was significantly associated with initial positive 24h UFC ( $\chi^2(4)=3.48$ ;  $p=0.481$ ) (**Table 1**).

A forced entry multiple regression revealed that phenotype was significantly related to the outcome (24-hour UFC value) ( $p=0.001$ ). Patients with Cushingoid phenotype had on average 24-hour UFC values 289.4 nmol above values recorded on patients with normal phenotype. A 95% confidence interval (CI) for this estimate was given by (164.0 - 414.9) (**Table 2**).



**Figure 1:** Indications of Requesting 24h UFC

**Table 1: Positive 24h UFC according to BMI records**

BMI (kg/m <sup>2</sup> )	Number of patients	Initial positive 24h UFC, n (%)	Final diagnosis of Cushing's syndrome, n (%)
<25	25	5 (20.0%)	3 (12.0%)
25-29.9	74	5 (6.8%)	0 (0.0%)
30-34.9	60	6 (10.0%)	1 (1.7%)
35-39.9	77	10 (13.0%)	1 (1.3%)
40+	89	7 (7.9%)	0 (0.0%)
Unavailable	31	3 (9.7%)	1 ((3.2%)
<b>Total</b>	<b>356</b>	<b>36 (10.1%)</b>	<b>6 (1.7%)</b>

$\chi^2_{(4)}=3.48$ ;  $p=0.481$

**Table 2: Results of 24h UFC according to patients phenotype**

	Cushingoid features present	Non-Cushingoid features present
<b>Number of patients</b>	31 (8.7%)	325 (91.3%)
<b>Positive 24h UFC, n (%)</b>	7 (22.6%)	29 (8.9%)
<b>Cushing's syndrome confirmed, n(%)</b>	4 (12.9%)	2* (0.6%)

\* These 2 patients have 24h UFC as part of adrenal incidentaloma workup

## Discussion:

24h UFC is commonly requested test to screen for secondary causes of obesity. Our study showed that BMI is not associated with positive 24h UFC. On the other hand, presence of classic Cushingoid features is strongly associated with positive 24h UFC results.

## Conclusion:

We did not find any benefit of requesting 24h UFC in those who did not have classic Cushingoid features. This audit confirms that we need to adhere to the Endocrine society guidelines on investigations for Cushing's syndrome.

## References:

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