Prevalence of Hypercortisolism in Patients With Adrenal Adenoma(s) and Type 2 Diabetes Mellitus: Findings From an Electronic Medical Records (EMR) Search

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INTRODUCTION

- Adrenal adenomas discovered incidentally during imaging are found in about 5% of the population, and their incidence increases with age[1]
- 5% to 30% of adrenal adenomas discovered during imaging are cortisol-secreting[2]
- Prevalence rates of hypercortisolism ranging from 2% to 9% have been reported in patients with type 2 diabetes mellitus (T2DM) who lack overt clinical features of cortisol excess (proximal muscle weakness, facial plethora, violaceous striae)[2-4]
- According to a meta-analysis of 32 studies (N=4,121) by Elhassan et al, patients with autonomous cortisol secretion have a high prevalence of cardiovascular risk factors (such as hypertension, obesity, dyslipidemia, and T2DM) and are more likely than those with nonfunctioning adrenal tumors to develop or show worsening of these factors during follow-up[1]
- Here we report the results of an investigator-initiated study on the prevalence of hypercortisolism in patients with T2DM and incidentally discovered adrenal adenomas. Clinical disease assessments (eg, glycated hemoglobin [HbA1c]) and medication use at baseline and after 1 year of follow-up are also examined.

METHODS

- A query of the electronic medical records (EMR) from 2014 to 2020 at NYC Health + Hospitals/Queens Diabetes Center was performed to identify patients ≥18 years old with radiologically confirmed adrenal adenoma(s) and a diagnosis of T2DM
  - ICD-10-CM codes used to identify patients were:
    - Diabetes mellitus type 2: E11.9
    - Adrenal mass/nodule: E27.9
- Excluded patients were those:
  - Taking exogenous systemic corticosteroids
  - Pregnant at the time computed tomography (CT) scan was performed
  - Having a life-threatening condition, including metastatic cancer
- Hypercortisolism was assessed using 1-mg dexamethasone suppression test (DST) with a diagnostic threshold of ≥1.8 μg/dL, either retrospectively (if available per EMR) or prospectively
  - Additional biochemical assessments to support diagnosis included adrenocorticotropic hormone (ACTH) and dehydroepiandrosterone-sulfate (DHEA-S)
  - All patients were required to have two CT scans 1 year apart to evaluate change in adenoma size
- The target enrollment was 30 patients
- At study initiation, 8 patients had completed both the required CT scans and evaluations for hypercortisolism
  - Twenty-two patients required additional biochemical testing and/or repeat imaging (CT scans >12 months prior to study visit), which were then obtained

RESULTS

- The study reached the target enrollment of 30 patients (**Figure 1**)

Figure 1. Patients

T2DM patients with adrenal adenoma enrolled
(N=30)

↓

Biochemical status
(N=30)

- Abnormal DST ≥1.8 μg/dL (n=13)
- Normal DST <1.8 μg/dL (n=17)

DST, dexamethasone suppression test; EMR, electronic medical records; T2DM, type 2 diabetes mellitus.

- The mean age of the patients was 64.9 years; 60% were female (**Table 1**)

Table 1. Demographic and Clinical Characteristics

Characteristic	Patients (N=30)
Male/female, n (%)	12 (40)/18 (60)
Age, years, mean (range)	64.9 (46-89)
HbA1c, %, mean (range)	7.3 (5.0-13.4)
Adrenal nodule size, cm, mean (range)	1.8 (1.1 to 5.1)
Systolic/diastolic blood pressure, mmHg, mean (range)	140 (110-231)/78 (68-109)

HbA1c, glycated hemoglobin.

- Thirteen patients (13/30, 43.3%) had an abnormal DST cortisol value ≥1.8 μg/dL (range: 1.9-8.0 μg/dL)
  - Eight of the these patients had validated ACTH results (range: 1.6-15.1 pg/mL) that supported an adrenal etiology for their hypercortisolism; the remaining 5 patients had ACTH values above the normal range using a different assay (Immulite)
  - Among the 13 patients with abnormal DST results, the adrenal nodule size ranged from 1.0 to 3.4 cm (**Table 2**)
- Seventeen patients (17/30, 56.7%) had a normal DST cortisol value (range 0.7-1.7 μg/dL)
  - Among these patients, the adrenal nodule size ranged from 1.0 to 5.1 cm (**Table 3**)

Table 2. Patients With Abnormal DST (cortisol ≥1.8 μg/dL)

Patient	1-mg DST (μg/dL)	Baseline HbA1c (%)	HbA1c After 1 Year (%)	Baseline BP (mmHg)	BP After 1 Year (mmHg)	Baseline CT Scan	CT Scan After 1 Year	ACTH (pg/mL)	Lab Assay	DHEA-S (μg/dL)
1	8.0	13.4	10.4	137/87	138/94	1.0-cm left adrenal nodule	No change	33.6	Immulite	27
2	3.9	6.6	8.8	110/70	114/73	1.3-cm right adrenal adenoma	1.8-cm right adrenal adenoma	36.1	Immulite	90.1
3	3.6	6.5	6.3	138/84	136/78	1.5-cm left adrenal nodule	1.8-cm left adrenal nodule	31.5	Immulite	87.7
4	3.4	6.2	6.3	133/87	138/74	1.1-cm left adrenal nodule	2.1-cm left adrenal nodule	20	Immulite	162
5	3.3	7.2	6.3	156/82	125/78	1.2 x 1.1 cm right adrenal nodule	1.3-cm right adrenal nodule	10	COBAS	25
6	3.0	5.0	6.1	146/72	136/56	1.0-cm left adrenal nodule	No change	14.8	COBAS	171
7	2.7	8.6	8.7	153/69	148/76	3.4-cm hypodense mass	3.3 x 2.4 right adrenal nodule	7	COBAS	<15
8	2.7	5.8	5.5	124/85	132/89	2.1 cm left adrenal nodule	No change	15	COBAS	182
9	2.2	7.2	7.1	130/70	138/80	2.4 x 1.7 cm nodule	2.4 cm nodule	10	COBAS	20
10	2.2	7.7	6.9	120/70	110/75	1.2-cm left adrenal nodule	No change	19	Immulite	18
11	2.0	7.7	6.9	145/89	134/78	Indeterminate right adrenal adenoma	Determinate right adrenal adenoma	8.9	COBAS	18
12	2.0	7.6	6.4	148/75	123/71	1.8-cm right adrenal nodule	2-cm right adrenal nodule	15.1	COBAS	46.7
13	1.9	7.8	8.0	130/86	167/90	2.1-cm left adrenal nodule	No change	1.6	COBAS	72

Normal values: ACTH Immulite assay, 6-58 pg/mL; ACTH COBAS assay, 7.4-64.3 pg/mL; DHEA-S for age >18 years, 89-457 μg/dL. ACTH, adrenocorticotropic hormone; BP, blood pressure; CT, computed tomography; DHEA-S, dehydroepiandrosterone-sulfate; DST, dexamethasone suppression test; HbA1c, glycated hemoglobin.

Table 3. Patients With Normal DST (cortisol <1.8 μg/dL)

Patient	1-mg DST (μg/dL)	Baseline HbA1c (%)	HbA1c After 1 Year (%)	Baseline BP (mmHg)	BP After 1 Year (mmHg)	Baseline CT Scan	CT Scan After 1 Year	ACTH (pg/mL)	DHEA-S (μg/dL)
1	1.7	7.0	7.5	140/80	145/95	1.1-cm right adrenal nodule	No change	10.9	27
2	1.6	8.0	7.4	139/92	129/81	1.0-cm left adrenal nodule	No change	15	18
3	1.5	7.8	6.5	132/68	128/59	2.5-cm left adrenal adenoma	No change	32	56
4	1.5	7.1	7.2	138/86	136/78	Left adrenal nodule	No change	9.4	21.6
5	1.4	5.6	7.9	142/88	170/100	1.1 x 1.0-cm left adrenal mass	No change	8.2	13.6
6	1.3	6.3	7.1	128/70	138/80	1.3-cm left adrenal nodule	No change	20.2	26
7	1.2	7.4	6.2	231/109	141/79	1.9-cm left adrenal nodule	No change	0.9	27.9
8	1.2	6.0	6.5	135/87	127/76	2.5 x 1.8 cm left adrenal nodule	No change	7.3	46.2
9	1.1	6.2	4.9	180/101	209/107	1.2-cm right adrenal nodule	No change	18	65.8
10	0.9	6.3	6.3	126/87	143/76	1.4 x 2.2-cm left adrenal nodule	No change	<15	15
11	0.8	8.0	5.8	158/79	111/71	Left adrenal nodule	No change	26.8	<5
12	0.8	6.8	4.2	139/85	118/84	1.9 x 1.0-cm left adrenal nodule	1.9 x 1.6-cm left adrenal nodule	19.4	31
13	0.8	5.7	5.8	126/81	170/100	1.5 x 1.4-cm right adrenal nodule	No change	19.4	31.4
14	0.7	8.6	4.6	168/80	166/79	1.5-cm left adrenal nodule	1.4-cm left adrenal nodule	45	49
15	0.7	7.2	7.2	145/71	179/84	5.1 x 3.5-cm right adrenal mass	No change	68	85.5
16	0.7	6.9	6.5	159/77	140/70	1.0-cm inferior pole nodule	No change	84	121
17	0.1	7.2	6.7	114/78	115/75	1.2 x 1.3-cm right adrenal mass	0.8-cm right adrenal mass	9.6	14.8

Normal values: ACTH, 6-64.3 pg/mL; DHEA-S for age >18 years, 89-457 μg/dL. ACTH, adrenocorticotropic hormone; BP, blood pressure; CT, computed tomography; DHEA-S, dehydroepiandrosterone-sulfate; DST, dexamethasone suppression test; HbA1c, glycated hemoglobin.

Medication Changes

- Compared with baseline medication use (**Table 4**), there were more medication dosage increases and new medications added to improve metabolic control of both diabetes and hypertension in the group with abnormal DST baseline values

Table 4. Number of Patients Taking Medications at Baseline for Diabetes and Hypertension

Patients	Diabetes	Hypertension	Both
Abnormal DST group (n=13)	11	13	9
Normal DST group (n=17)	15	15	14

- Abnormal DST cortisol ≥1.8 μg/dL group (n=13):
  - 10/13 (76.9%) patients had an increase in the dosage of their diabetes medications and/or were prescribed a new medication for diabetes
  - 10/13 (76.9%) patients had an increase in the dosage of their blood pressure medications and/or were prescribed a new medication for blood pressure
  - 1 patient had a reduction in the number and/or dosage of diabetes and blood pressure medications, 1 patient had a reduction in the number of blood pressure medications, and 1 patient had no medication changes at all
- Normal DST cortisol <1.8 μg/dL group (n=17):
  - 5/17 (29.4%) patients had an increase in the dosage of their diabetes medications and/or were prescribed a new medication for diabetes
  - 2/17 (11.8%) patients had an increase in the dosage of their blood pressure medications and/or were prescribed a new medication for blood pressure
  - 4 patients had a decrease in dosage or discontinuation of diabetes medications, 2 patients had a decrease in dosage or discontinuation of blood pressure medications, and 1 patient had a dosage decrease or discontinuation of both

DISCUSSION/CONCLUSION

- Broad use and technical advances in abdominal imaging procedures have led to the discovery of unsuspected adrenal adenomas at an increasing frequency. These adrenal "incidentalomas" have been increasingly shown to be associated with clinical complications, leading to guidelines recommending evaluation of hormonal hypersecretion and/or malignancy. Currently, these recommendations are often not followed.
- The prevalence of cortisol-secreting adenomas in patients with T2DM was 43.3% in this study, which is higher than previously reported rates[2-4]
  - Patients who had an abnormal DST result (cortisol ≥1.8 μg/dL) at baseline required more medication adjustments and changes due to worsening control of their diabetes and hypertension
- Recommendations
  - The use of EMR, when combined with common manifestations associated with hypercortisolism (in this case, diabetes), can increase the detection of potentially treatable autonomous cortisol secretion in patients with adrenal adenomas

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