



## Background

- Because persistent fever often occurs in adrenal insufficiency, it might be confused with infectious diseases in the real-world setting.
- As a result, patients with adrenal insufficiency and fever might not receive proper treatment timely, leading to prolonged hospitalization as well as the unnecessary use of antibiotics.
- The aim of the present study is to analyze the clinical characteristics of adrenal insufficiency patients presenting fever.

## Methods

### • Study design

- A single-center retrospective study (846-bed tertiary-care hospital)
- Study period: Mar 2018 – Jun 2019

### • Inclusion criteria

- Adult hospitalized patients (≥19 years)
- Diagnosed with adrenal insufficiency during hospitalization

\* Post-ACTH stimulation cortisol level (30 min and 60 min) < 20mcg/dL

### • Exclusion criteria

- Existence of proven structural problems with adrenal or pituitary gland
- Existence of history of chemotherapy within 6 months prior to the diagnosis of adrenal insufficiency
- Existence of other medical conditions which may cause fever

### • Definition of groups

- Case group: tympanic temperature ≥37.8°C (at the time of diagnosis)
- Control group: tympanic temperature <37.8°C (at the time of diagnosis)

## Results

- A total of 150 cases were included
  - 45 (30.0%) had fever and 105 (70.0%) did not have fever

Table 1. Comparison of clinical characteristics of adrenal insufficiency patients presenting fever to those without fever

	Case (n = 45)	Control (n = 105)	P	Total (n = 150)
<b>Demographic data</b>				
Age, mean±SD	72.60±12.14	69.45±15.51	0.184	70.39±14.61
Female sex (%)	20 (44.4)	71 (67.6)	0.008	91 (60.7)
Hospital days at the time of diagnosis, mean ± SD	13.98±14.51	6.47±6.91	<0.001	8.72±10.36
Charlson's comorbidity index score	2.42±1.89	2.82±2.23	0.333	2.55±2.01
<b>Medical histories</b>				
Renal replacement therapy (%)	4 (8.9)	6 (5.7)	0.488	10 (6.7)
History of infectious disease within 1 month (%)	12 (26.7)	16 (15.2)	0.100	28 (18.7)
History of surgical procedure within 6 months (%)	15 (33.3)	12 (11.4)	0.001	27 (18.0)
Prior use of corticosteroid (%)	16 (35.6)	40 (38.1)	0.768	56 (37.3)
Use of corticosteroid (%)	13 (28.9)	34 (32.4)	0.673	47 (31.3)
Use of antibiotics (%)	36 (80.0)	18 (17.1)	<0.001	54 (36.0)
Use of Immunosuppressant (%)	9 (20.0)	23 (21.9)	0.794	32 (21.3)
<b>Clinical manifestations</b>				
General weakness (%)	41 (91.1)	70 (66.7)	0.002	111 (74.0)
Confusion (%)	3 (6.7)	10 (9.5)	0.755	13 (8.7)
Headache (%)	7 (15.6)	5 (4.8)	0.044	12 (8.0)
Dizziness (%)	5 (11.1)	14 (13.3)	0.708	19 (12.7)
Skin rash (%)	1 (2.2)	3 (2.9)	1.000	4 (2.7)
Edema (%)	11 (24.4)	15 (14.3)	0.132	26 (17.3)
Myalgia (%)	11 (24.4)	14 (13.3)	0.094	25 (16.7)
Abdominal pain (%)	9 (20.0)	20 (19.0)	0.892	29 (19.3)
Nausea (%)	21 (46.7)	51 (48.6)	0.831	72 (48.0)
Vomiting (%)	11 (24.4)	37 (35.2)	0.194	48 (32.0)
Diarrhea (%)	7 (15.6)	11 (10.5)	0.380	18 (12.0)
Constipation (%)	4 (8.9)	10 (9.5)	1.000	14 (9.3)
Hepatosplenomegaly (%)	1 (2.2)	1 (1.0)	0.511	2 (1.3)
Chest pain (%)	3 (6.7)	3 (2.9)	0.365	6 (4.0)
Cough (%)	8 (17.8)	5 (4.8)	0.022	13 (8.7)
Dyspnea (%)	5 (11.1)	13 (12.4)	0.826	18 (12.0)

Table 2. Comparison of clinical outcomes of adrenal insufficiency patients presenting fever to those without fever

	Case (n = 45)	Control (n = 105)	P	Total (n = 150)
Defeverence days after steroid supplement, mean ± SD	3.25 ± 1.68	-	-	-
CRP at 3 days after steroid supplement, mean ± SD	4.94 ± 3.97	-	-	-
CRP at 7 days after steroid supplement, mean ± SD	3.62 ± 3.27	-	-	-
All-causes mortality at 30 days after admission (%)	1 (2.2)	2 (1.9)	1.000	3 (2.0)
Hospitalization duration from diagnosis, mean ± SD	18.27 ± 25.25	11.48 ± 17.95	0.064	13.48 ± 20.52

Table 3. Risk factors for adrenal insufficiency presenting fever

	Univariate analysis			Multivariate analysis	
	No.	OR (95% CI)	P	OR (95% CI)	P
<b>Age &gt;70</b>					
No	38	1.00	-	-	-
Yes	68	1.25 (0.53-2.97)	0.606	-	-
<b>Female sex</b>					
No	42	1.00	-	1.00	-
Yes	64	0.37 (0.16-0.86)	0.020	0.32 (0.12-0.86)	0.024
<b>Charlson's comorbidity index &gt;2</b>					
No	76	1.00	-	-	-
Yes	30	1.33 (0.55-3.25)	0.525	-	-
<b>History of infectious diseases within 1 month</b>					
No	84	1.00	-	-	-
Yes	22	2.08 (0.79-5.46)	0.135	-	-
<b>History of surgical procedure within 6 months</b>					
No	85	1.00	-	1.00	-
Yes	21	2.97 (1.11-7.91)	0.030	4.35 (1.23-15.39)	0.023
<b>General weakness</b>					
No	28	1.00	-	1.00	-
Yes	78	5.50 (1.53-19.78)	0.009	7.21 (1.71-30.37)	0.007
<b>Headache</b>					
No	97	1.00	-	1.00	-
Yes	9	2.93 (0.73-11.71)	0.128	4.11 (0.79-21.27)	0.092
<b>Myalgia</b>					
No	86	1.00	-	-	-
Yes	20	2.58 (0.96-6.99)	0.062	-	-
<b>Cough</b>					
No	100	1.00	-	1.00	-
Yes	6	0.08 (0.00-0.73)	0.025	17.29 (1.09-274.92)	0.043

**Conclusions:** Approximately 30% of adrenal insufficiency patients presented fever. The possibility of adrenal insufficiency should be considered in patients with fever of unknown origin and risk factors such as male sex, a history of surgery within 6 months, general weakness, and cough.