

1 **Clinical utility of urinary ratio of free cortisol to aldosterone as an index**
2 **for inflammatory and metabolic dysregulation.**

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12 **Running Title:** Ratio of urinary free-cortisol to aldosterone

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Abstract

25 **Background:** Urinary free cortisol (UFC) is a reliable marker to avoid cortisol fluctuation
26 and effects of binding proteins. However, UFC levels are affected by fluid intake or
27 urine volume, and the normal levels range widely. **Methods:** To know the utility of the
28 ratio of urinary cortisol to aldosterone excretions, 246 patients in whom daily excretions
29 of UFC and aldosterone (UAC) were measured were retrospectively analyzed. **Results:**
30 UFC/UAC ratio showed significant positive and negative correlations with the levels of
31 serum cortisol ($R=0.287$) and aldosterone ($R=-0.762$), respectively. UFC/UAC ratio
32 increased with aging in female patients, while that was not altered by the levels of BMI
33 in either gender. Markers for metabolic and inflammatory status including hemoglobin
34 A1c ($R=0.327$), albumin ($R=-0.331$), C-reactive protein ($R=0.317$), ferritin ($R=0.473$),
35 and D-dimer ($R=0.569$) showed correlations to the ratio of UFC/UAC that were more
36 significant than the correlations to the serum level of cortisol or UFC alone. Of note,
37 the UFC/UAC ratio was shown as an indicator for risks of diabetes (AUC: 0.765),
38 hypoalbuminemia (0.839), hyper-CRPemia (0.748), and thrombophilia (0.824), in which
39 the cut-off levels of UFC/UAC ratios were around 12. **Conclusions:** The UFC/UAC
40 ratio is a variable for detecting metabolic and inflammatory complications related to
41 adrenocortical dysfunction. (200 words).