

# Prolonged Fasting as a Trigger for Adrenal Crisis in a Non-Muslim Sub-Saharan African: Case Report

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**Abstract:** Addison's disease, or primary adrenal insufficiency, is a rare but potentially life-threatening endocrine disorder. Adrenal crisis may occur when patients are exposed to physiological stressors such as infection, trauma, or fasting, especially in the context of poor treatment adherence. Although fasting-related adrenal crisis is typically associated with Muslim patients during Ramadan, reports among non-Muslim individuals are exceedingly rare. We describe a 37-year-old black male, Christian, from sub-Saharan Africa, with a known diagnosis of Addison's disease on oral glucocorticoid therapy, who presented with worsening asthenia, hypotension, and vomiting after a prolonged fasting period motivated by personal religious beliefs. The patient reported irregular medication adherence and had not increased the glucocorticoid dose during the fasting period. The patient was diagnosed with adrenal crisis secondary to prolonged fasting and poor adherence and improved rapidly after intravenous hydrocortisone and fluid replacement. Our case suggests that patients with Addison's Disease are at higher risk of developing adrenal crisis during fasting periods. Close monitoring and adjustments of the therapy are recommended.

**Keywords:** Adrenal Crisis; Fasting; Non-Muslim; African Sub-Saharan.

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## 1. Introduction

Addison disease was initially described by Thomas Addison in 1855 as an acquired primary adrenal insufficiency (PAI) that leads to decreased production of cortisol, aldosterone and androgens [1,2]. It is a rare condition with a reported prevalence of 100 to 140 cases per million and an incidence of 4 to 6 per million per year in adults [3]. Autoimmune adrenalitis is the main cause accounting for 90% of cases in developed countries followed by infections such as tuberculosis. Other etiologies include shock, HIV, tumor, infiltration, trauma/surgery, medications and adrenal hemorrhage [4].

Adrenal crisis is a life threatening condition characterized by acute severe cortisol and/or mineralocorticoids deficiency that present with non-specific symptoms such as severe fatigue, dizziness, vomiting, abdominal pain, hemodynamic disturbance (hypotension or sinus tachycardia), electrolyte abnormality (e.g., hyponatremia, hyperkalemia, hypoglycemia), shock and coma that resolves within 1 to 2 hours after glucocorticoid administration [5]. This condition may be triggered by stressful factors such as infections, gastroenteritis, trauma, severe illness, surgery, emotional distress and non-adherence to glucocorticoids in previous diagnosed patients [5,6]. Prolonged Fasting has been described

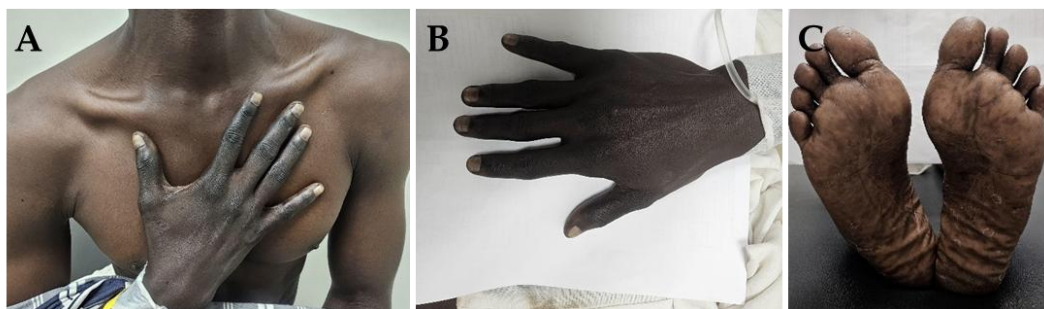
as a risk factor for adrenal crisis in muslim population during Ramadan, on the other hand it is poorly studied in non-muslim population [7].

## 2. Case Report

We present a case of a 37 years old non-muslim (Christian) black male with previous diagnosis of Addison's Disease 6 years ago medicated with oral hydrocortisone 25 mg per day with irregular adherence (days, <30% of prescribed dose) initially asymptomatic that referred extreme fatigue, weight loss (>40 kg), anorexia and accentuation of skin hyperpigmentation (Figure 1) after 4 weeks of fasting with intermittent food and water restriction, without adjustment of medication dosage and with irregular compliance.

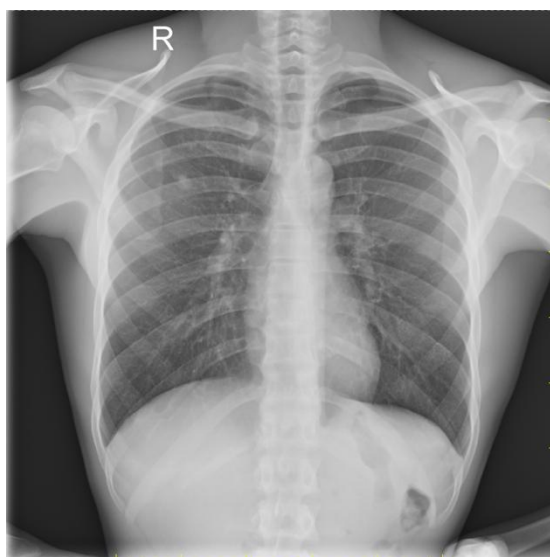
Before hospital admission, the patient presented intense abdominal pain, multiple vomiting episodes, asthenia and a syncopal episode. At the entrance the patient was lethargic, non-responsive, with pale and dehydrated mucous membranes, hypotensive (80/64 mmHg) and tachycardic (>120 bpm) with clinical signs of circulatory shock despite adequate IV volume reposition. Physical examination revealed heterogenous skin hyperpigmentation (Figure 1) without another relevant findings.

**Figure 1.** Heterogenous skin hyperpigmentation (A. neck, thorax and right hand, B. right hand; C. Feet – sole region).

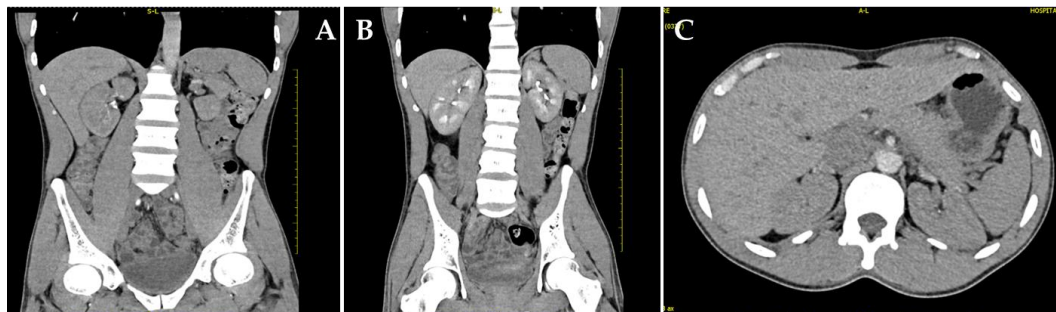


Lab results showed electrolyte imbalance with moderate hyponatremia (123mmol/L), mild hyperkalemia (5.3 mmol/L), serum glucose was 74 mg/dL and hemogram revealed moderate anemia (9.6g/dL), neutropenia (26.4%) with lymphocytosis (59.3%). Urea, creatinine, transaminases were normal with negative serology (CMV, VLDR, HIV). Chest X-ray was normal (Figure 2) and Contrast enhanced Abdominal CT (Figure 3) did not reveal any structural abnormality in both adrenal glands. Despite recommendation, we could not perform serum ACTH and cortisol measurement due to unavailability of laboratory reagents and corresponding test kits during the study period.

**Figure 2.** Anterior-posterior normal chest X-ray.



**Figure 3.** A. Coronal view, contrast enhanced Abdominal CT. Right adrenal glands with no relevant findings (see yellow arrow). B. Coronal view, contrast enhanced Abdominal CT. Left adrenal glands with no relevant findings (see yellow arrow) and C. Axial view, contrast enhanced Abdominal CT. Right adrenal glands with no relevant findings (see yellow arrow).



The patient was treated for adrenal crisis with IV hydrocortisone and fluid replacement, with clinical and laboratory improvement [blood glucose (74 - 91.7mg/dL); hemogram (Neutrophil 26.4 - 72.7%; Lymphocytes 59.3 - 21.4%, hemoglobin 9.6g/dL - 11.3g/dL) and electrolyte normalization (Sodium 123 mmol/L - 134 mmol/L; Potassium 5.3 mmol/L - 3.8 mmol/L)] and was discharged after 10 days of hospitalization.

### 3. Discussion

Fasting causes various alterations in body normal functioning and physiological mechanisms such as hepatic glycogenolysis, lipolysis and gluconeogenesis are activated to maintain normal blood glucose levels [8]. During the first hours of fasting glycogenolysis is activated and hepatic and muscle glycogen is catabolized to maintain optimal glucose levels. If fasting continues gluconeogenesis is also activated and glucose is synthesized through non-carbohydrate substrates as lactate, amino-acids and glycerol [9,10]. These metabolic pathways maintain body homeostasis and are regulated by stimulating hormones such as cortisol and glucagon and by inhibitory hormones as insulin [11].

Cortisol is a steroid hormone produced by the adrenal glands and is controlled by hypothalamus and pituitary gland axis and increases glucose availability and uptake to the brain by stimulating gluconeogenesis and acting on organs as liver, muscle and adipose tissue [12]. In liver, cortisol stimulates gluconeogenesis [10]; in muscles, it plays an important role by decreasing glucose uptake and consumption and increasing protein breakdown [12–14]; and in adipose tissue it stimulates the breakdown of triglycerides into fatty acids and glycerol [12,13]. Therefore, during fasting glucose blood level drops and cortisol demands increase to maintain stable blood glucose levels and contribute to energy homeostasis [12]. Cortisol also plays an important role on vascular tonus by increasing vasoconstriction and reactivity which increases blood pressure in acute stress [1].

It also has an important anti-inflammatory effect on immune cells and in acute stress leads to increase neutrophil recruitment and lifespan and decreased circulating lymphocytes [15]. In hypocortisolism as in Addison disease the adaptive response to fasting is compromised and these patients develop hypoglycemia, asthenia and hypotension and it may also precipitate an adrenal crisis as observed in our patients.

The relation between fasting and the onset of adrenal crisis is not yet fully understood however some studies have shown that it can be considered as a cause of complications among patients with adrenal insufficiency [16]. There are few reports of patients with known Addison disease that developed adverse effects after religious fasting during Ramadan. In these patients, clinical manifestations such as asthenia, intense thirst, symptoms of dehydration, hypoglycemia and a preference for salty foods were also reported [16,17].

Our case report presents a non-muslim (Christian) patient that developed severe abdominal pain, multiple vomiting episodes, asthenia, hypoglycemia and clinical signs of

volume depletion after prolonged fasting period. This alteration can be attributed to cortisol deficiency reflecting maladaptive homeostatic response to fasting.

Aldosterone deficiency is also common in patients with Addison's disease. It leads to reduced water and sodium reabsorption as well as reduced potassium secretion resulting in volume depletion and electrolytes imbalance as hyponatremia and hyperkalemia [18,19]. These abnormalities were also present in our clinical case in which the patient was admitted to the emergency room with clinical signs of volume depletion as hypotension, dehydration, lethargy with clinical signs of circulatory shock. Besides, the patient also presented electrolyte imbalance such as hyponatremia (123 mmol/L) and hyperkalemia (5.3mmol/L) that were resolved during hospitalization after IV hydrocortisone administration.

Literature states that during fasting these patients are at higher risk of developing adverse events. To avoid it adjustment in their therapy and careful monitoring are recommended [17]. Several strategies for preventing adrenal crises have been extensively evaluated for implementation and use in patients, such as individualized medical prescription, doubling or tripling the dose of oral glucocorticoids depending on the stress to which the patient will be exposed, or even the use of parenteral glucocorticoids in cases of severe stress. Specifically for patients with adrenal insufficiency who wish to fast, recommendations have been provided, not only to guide the patients themselves, but also the healthcare professionals who deal with them in such situations [20]. These recommendations are particularly relevant as they emphasize the need for patient risk stratification, review of the individualized treatment plan during the fasting period, and, above all, education about the disease and its behavior in this context [20,21]. They also include guidelines on when to abstain from or interrupt fasting in the event of signs of serious complications, as well as training in the intramuscular administration of hydrocortisone in the event of such complications [5,20].

This clinical case highlights the need for close monitoring of patients with Addison's disease during fasting due to the risk of serious complications when follow-up is inadequate. In addition, this case reinforces the importance of encouraging therapeutic adherence, since the patient not only failed to adjust his medication during fasting, but also had irregular adherence to his usual therapy, which further aggravated his clinical condition. Active patient participation in disease management, especially during this period, is essential, as these patients are more susceptible to complications during fasting if their knowledge of the disease is low [17].

#### 4. Conclusion

In summary, fasting can precipitate adrenal crisis even outside the usual cultural or religious contexts. Clinicians should proactively counsel all patients with adrenal insufficiency about the potential risks of fasting and the necessity of medication compliance and dose adjustment during physiological stress. We acknowledge that despite diagnostic limitations due to lack of ACTH and Cortisol measurement during the study period the clinical picture strongly supports the conclusion and proactive patient counselling is mandatory.

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**Conflicts of Interest:** All other authors declare no conflicts of interest.

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