Reconsidering Glucocorticoid-Induced Hyperglycemia as a Distinct Pathophysiological Entity: Implications for Inpatient Glycemic Protocols in Non-Diabetic Critically Ill Patients

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Abstract. Glucocorticoid-induced hyperglycemia (GIH) has historically been managed under frameworks designed for pre-existing diabetes mellitus, yet mounting evidence suggests this conflation carries significant clinical risk. This study examined the pathophysiological divergence of GIH from type 2 diabetes in 312 non-diabetic critically ill patients receiving systemic corticosteroid therapy across three tertiary care centers. Using continuous glucose monitoring, hyperinsulinemic-euglycemic clamp studies, and β-cell secretory profiling, we characterized unique postprandial glucose excursions and relative insulin resistance patterns specific to GIH. Multivariate regression identified corticosteroid dose, administration timing, and hepatic glucose output as primary modulators. Our findings challenge the universal applicability of standard inpatient glycemic targets and advocate for GIH-specific titration protocols, with observed reductions in hypoglycemic episodes and length-of-stay when tailored interventions were applied.

Keywords: glucocorticoid-induced hyperglycemia, inpatient glycemic management, critical illness endocrinopathy, corticosteroid-associated insulin resistance, β-cell dysfunction, postprandial glucose excursion, non-diabetic hyperglycemia, euglycemic clamp, tertiary care glycemic protocol

Introduction

Dysglycemia in the critically ill patient represents one of the most consequential and underappreciated challenges in contemporary inpatient medicine. While the landmark NICE-SUGAR trial reshaped global glycemic targets in intensive care units, its framework was constructed predominantly around patients with established diabetes mellitus or stress hyperglycemia of non-pharmacological origin. A critical and growing subpopulation—those experiencing glucocorticoid-induced hyperglycemia (GIH) in the absence of pre-existing glucose metabolism disorders—has been systematically subsumed within these generalized protocols, often to their detriment. As of 2024–2026, systemic corticosteroid use continues to escalate across clinical contexts including autoimmune exacerbation, post-transplant immunosuppression, septic shock management per Surviving Sepsis Campaign guidelines, and malignancy-associated inflammation. The resulting GIH burden in non-diabetic inpatients is estimated to affect between 20% and 46% of all corticosteroid-treated hospitalized adults, yet institutional response protocols remain largely undifferentiated from those applied to established diabetic patients. The pathophysiology of GIH is mechanistically distinct from classical type 2 diabetes mellitus. Glucocorticoids exert pleiotropic metabolic effects including impairment of peripheral glucose transporter type 4 (GLUT-4) translocation, augmentation of hepatic gluconeogenesis via phosphoenolpyruvate carboxykinase (PEPCK) upregulation, attenuation of first-phase insulin secretion, and induction of lipotoxic intermediaries that compromise pancreatic β-cell viability. These mechanisms produce a characteristic diurnal hyperglycemic signature—predominantly postprandial and afternoon-dominant—that diverges substantially from the fasting-predominant hyperglycemia observed in type 2 diabetes. Standard sliding-scale insulin regimens and fixed basal-bolus protocols calibrated for the latter phenotype therefore introduce systematic mismatch when applied to GIH, potentially precipitating nocturnal hypoglycemia while permitting clinically significant postprandial excursions. Despite growing recognition of GIH as a distinct clinical entity within endocrinology subspecialty literature, its formal reclassification within critical care glycemic governance documents has been slow and inconsistent across international guidelines. This gap between mechanistic understanding and institutional protocol design constitutes a patient safety concern of measurable magnitude, particularly as corticosteroid prescribing patterns have intensified in the post-COVID-19 therapeutic landscape. The present article is structured as follows: Section 2 details patient selection criteria, continuous glucose monitoring methodology, and clamp study protocols; Section 3 presents the comparative glycemic profiling results stratified by corticosteroid class, dose, and administration timing; Section 4 offers a mechanistic synthesis of observed insulin resistance and secretory deficit patterns; Section 5 proposes a GIH-specific glycemic management algorithm for non-diabetic critically ill patients; and Section 6 addresses study limitations and future research directives.

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