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Review Article

## Enhancing Diabetes Care: Strategies for Preventing Inpatient Hypoglycemia

**Rosmin Jacob<sup>1</sup>, Blessy Biju<sup>2</sup>, Dr. L. Panayappan<sup>3</sup>, Dr. Rajesh Kumar Sharma<sup>4</sup>**<sup>1</sup> Ph.D. scholar, Nims Institute of Pharmacy, Nims University Rajasthan, Assistant Professor, Department of Pharmacy Practice, St James College of Pharmaceutical Sciences, Chalakudy, Kerala.<sup>2</sup> Pharm D, St James College of Pharmaceutical Sciences, Chalakudy, Kerala.<sup>3</sup> Professor, Department of Pharmacy Practice, St James College of Pharmaceutical Sciences, Chalakudy, Kerala.<sup>4</sup> Associate professor, Nims Institute of Pharmacy, Nims University Rajasthan.

### ABSTRACT

Hypoglycemia, a common complication of diabetes treatments among hospitalized patients, poses significant risks, including increased morbidity, longer hospital stays, higher readmission rates, and greater financial burdens. In the hospital setting, hypoglycemia poses a significant challenge, impacting patient health and healthcare resources. This review dives deep into this issue, shedding light on the many factors contributing to hypoglycemia during hospital stays and its effects on patients. It emphasizes practical strategies for preventing hypoglycemia, such as patient education and the use of new technologies like continuous glucose monitoring. Additionally, it highlights the crucial role pharmacists play in managing hypoglycemia and improving patient care. By offering clear insights and actionable recommendations, this review aims to help healthcare providers better navigate the complexities of inpatient diabetes care for improved patient outcomes.

**Keywords:** diabetes, insulin, metabolic disorder, inpatient hypoglycemia, risk factors, prevention, hospitalization, pharmacist's role.

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\*Address for Correspondence:

Rosmin Jacob, Ph.D. scholar, Nims Institute of Pharmacy, Nims University Rajasthan, Assistant Professor, Department of Pharmacy Practice, St James College of Pharmaceutical Sciences, Chalakudy, Kerala.

### INTRODUCTION

Hypoglycemia, a common complication of diabetes treatments among hospitalized patients, poses significant risks, including increased morbidity, longer hospital stays, higher readmission rates, and greater financial burdens.<sup>1</sup> It's crucial to note that hypoglycemia can affect both diabetic and non-diabetic individuals in hospital settings, and while it's linked to higher mortality rates, it often signals an underlying health issue rather than being the direct cause of death. Nonetheless, it remains a serious consequence of metabolic dysfunction and diabetes management. Hence, it's important to minimize its occurrence during hospitalization for better patient outcomes.<sup>2</sup> Hypoglycaemia prevention begins with assessing an individual's history and risk factors. Structured patient education plays a vital role in improving hypoglycemia outcomes.<sup>3</sup> Blood glucose monitoring (BGM) and continuous glucose monitoring

(CGM) are crucial tools for managing diabetes. The advent of diabetes technology has introduced automated insulin delivery (AID) systems, where CGM data inform algorithms to adjust insulin delivery. Connected insulin pens and diabetes self-management support software further enhance patient care.<sup>4</sup> Pharmacists contribute to rational drug selection and enhance patient awareness of hypoglycemia, providing tailored education and protocols for prevention and treatment. They optimize insulin and non-insulin therapies, recommend alternatives for high-risk patients, and ensure access to glucagon kits, directing patients to relevant resources for additional support.<sup>5</sup> Collaboration between healthcare professionals is key to addressing the complexities of inpatient hypoglycemia and enhancing patient care in hospital settings.

## Hypoglycaemia classification

The ADA defines hypoglycemia according to 3 levels. Level 1 hypoglycemia is defined as a blood glucose concentration between 54 mg/dL (3.0 mmol/L) and 70 mg/dL (3.9 mmol/L). Even without symptoms, a glucose level below 70 mg/dL is considered clinically important, especially for individuals with impaired awareness. Level 2 hypoglycemia (blood glucose <54 mg/dL [3.0 mmol/L]) triggers neuroglycopenic symptoms and requires immediate action. If someone experiences level 2 hypoglycemia without symptoms, it may indicate impaired awareness, necessitating a review of the treatment plan. Lastly, level 3 hypoglycemia is severe, leading to altered mental or physical functioning requiring assistance for recovery, regardless of glucose level. Level 3 hypoglycemia may be recognized or unrecognized and can progress to loss of consciousness, seizure, coma, or death. It is characterized by altered mental or physical functioning requiring assistance for recovery, regardless of glucose level.<sup>3</sup>

Another classification of hypoglycemia revolves around its occurrence within specific contexts. Primary hypoglycemia occurs when low blood sugar levels are the primary reason for a patient's admission. On the other hand, secondary hypoglycemia refers to episodes that happen during hospitalization, sometimes termed inpatient hypoglycemia. Further delineating hypoglycemia during hospitalization, can be categorized into spontaneous and iatrogenic types. Spontaneous hypoglycemia may manifest in diabetic patients with multiple organ failure, malnutrition, or a history of drug consumption, all of which predispose individuals to hypoglycemic episodes. In contrast, iatrogenic hypoglycemia arises from overly aggressive treatment of hyperglycemia, coupled with the body's inability to respond to declining blood glucose levels appropriately. This condition, termed Hypoglycemia-Associated Autonomic Failure (HAAF), is observed in various contexts, including type 1 diabetes, severe comorbid diseases, advanced age, and individuals with a history of recurrent hypoglycemia.<sup>6</sup>

## The risk factors of inpatient hypoglycemia

Hypoglycemia is the most common complication of diabetes therapy in hospitalized patients. Individuals treated with insulin, sulfonylureas, or meglitinides are at risk of hypoglycemia, with the highest rates observed among those undergoing intensive insulin therapy, followed by basal insulin, and then sulfonylureas or meglitinides. Additionally, combining insulin and sulfonylureas further heightens the risk of hypoglycemia. Clinical and biological risk factors for hypoglycemia include recent level 2 or 3 hypoglycemia within the past 3–6 months, intensive insulin therapy, impaired hypoglycemia awareness, end-stage kidney disease, and cognitive impairment or dementia. Other contributing factors encompass multiple recent episodes of level 1 hypoglycemia, basal insulin therapy, being aged 75 or older, female gender, high glycemic variability, polypharmacy, cardiovascular disease, chronic kidney disease (eGFR <60 mL/min/1.73 m<sup>2</sup> or albuminuria), neuropathy, retinopathy, and major depressive disorder. Social, cultural, and economic risk factors for hypoglycemia encompass major factors such as food insecurity, low-income status, homelessness, and fasting for religious or cultural reasons. Additional risks include low

health literacy and alcohol or substance use disorder.<sup>3</sup> Insulin is the primary treatment for high blood glucose levels in both critically and non-critically ill patients, but it also poses risks for adverse events. Errors in insulin dosing, missed doses, and administration errors are common, involving prescriber, pharmacy, and nursing errors. Common preventable sources of hypoglycemia include improper prescribing of glucose-lowering medications and inadequate management of the first hypoglycemic episode.<sup>2</sup>

Kidney failure increases the risk of hypoglycemia in hospitalized patients due to decreased insulin clearance. Managing blood glucose levels in diabetic patients with end-stage renal failure is challenging due to factors such as metabolic acidosis and uremia, which increase insulin resistance. Post-dialysis patients may also experience fluctuating insulin resistance and increased insulin degradation, complicating glycemic control.<sup>7</sup> Iatrogenic hypoglycemia can be induced by factors such as corticosteroid dose reductions, reduced oral intake, vomiting, inappropriate timing of insulin doses, reduced intravenous dextrose infusion rates, interruptions in feeding, delayed blood glucose checks, and impaired symptom reporting.<sup>2</sup> Pediatric and elderly patients are highly vulnerable to hypoglycemia due to decreased recognition of symptoms and impaired communication. Elderly patients also experience reduced counter-regulatory hormonal responses and autonomic nerve function during hypoglycemia, exacerbating their vulnerability.

Hypoglycemia in hospital settings can stem from a variety of sources. Individual factors, such as the patient's age, the presence of severe comorbidities like sepsis or renal impairment, and other endocrine disorders, play a significant role. Additionally, management practices, such as overly aggressive hyperglycemia treatment and changes in dietary intake, can contribute to hypoglycemic episodes. Institutional factors, like inadequate blood glucose monitoring, unclear medical instructions, and communication gaps between healthcare teams, also play a crucial role in hypoglycemia occurrence. Addressing these multifaceted factors comprehensively is essential for effectively managing and preventing hypoglycemia in hospital settings.<sup>4</sup> Physiological and pharmacological factors contributing to hypoglycemia risk in hospitals include conditions like acute kidney injury, liver failure, and sepsis, as well as changes in medications that affect glucose levels. Environmental factors, such as limited food availability and prolonged fasting times, also play a role. Inappropriate diabetes management practices, including excessive use of intravenous insulin infusion and medication errors, further contribute to hypoglycemia risk.<sup>8</sup>

## The burden of inpatient hypoglycemia

Good glycemic control is crucial for reducing both macrovascular and microvascular complications in diabetic patients. However, hypoglycemia poses a significant obstacle to achieving this goal and imposes a substantial economic burden on healthcare systems. A study conducted in China found that hypoglycemia is a common occurrence among insulin-treated patients in Chinese hospitals. This burden is associated with increased utilization of medical resources and expenditures, particularly in cases of severe

hypoglycemia, which is prevalent among insulin-treated diabetes patients in China.<sup>9</sup>

Inpatient hypoglycemia has been linked to adverse health outcomes, including higher mortality rates, especially when hypoglycemia is severe. Research indicates a short-term mortality rate of 2.6% among hypoglycemic admissions. Severe hypoglycemia has also been shown to increase the risk of acute coronary syndrome, particularly in older adults aged 70 or older and within the first 10 days after the hypoglycemic event. Additionally, frequent exposure to hypoglycemia may elevate the risk of stroke and contribute to in-hospital falls.<sup>1</sup>

Moreover, hypoglycemia is associated with longer hospital stays, even after adjusting for the number of glucose tests performed. A recent meta-analysis revealed that inpatients exposed to hypoglycemia had an average of 4.1 days longer hospital stay.<sup>9</sup> The DIAMOND study further highlighted the higher mortality rates among diabetic patients experiencing hypoglycemia during hospitalization, along with longer hospital stays compared to those who did not experience hypoglycemic episodes.<sup>10</sup> A retrospective study investigated hypoglycemia in 324 hospitalized type 2 diabetes patients. Results revealed hypoglycemia associated with advanced age, insulin therapy, higher comorbidity index, lower BMI, and baseline HbA1c. Hypoglycemia correlated with increased in-hospital and long-term mortality, longer stays, higher readmission rates, and poorer post-discharge metabolic control. Prevention measures are crucial for vulnerable patients with type 2 diabetes experiencing hypoglycemia during hospitalization.<sup>11</sup>

Hypoglycemia is common in both type 1 and type 2 diabetes, especially in patients on insulin or sulfonylureas, and is linked to significant cardiovascular effects. Proposed mechanisms include hemodynamic changes, myocardial ischemia, abnormal cardiac repolarization, and inflammation, fostering endothelial dysfunction and atherogenesis. While causality remains uncertain, newer diabetes medications offer cardiovascular benefits without hypoglycemia. Technologies like continuous glucose monitoring and insulin pumps help reduce hypoglycemia.<sup>12</sup>

### Prevention and management of inpatient hypoglycemia

Preventing inpatient hypoglycemia is achievable through proactive measures like regular blood glucose monitoring, ensuring adequate dietary intake, and adjusting insulin doses based on patient's condition. Physicians must also be vigilant in recognizing risk factors such as insulin/sulfonylurea therapy, IV insulin for high potassium, multiple organ failure/sepsis, prior hypoglycemia history, and the use of non-diabetic drugs causing low blood sugar. By addressing these factors, we can effectively reduce the occurrence of hypoglycemia during hospitalization and ensure safer patient care.<sup>13</sup>

Hypoglycemia prevention begins with assessing an individual's history and risk factors. Structured patient education plays a vital role in improving hypoglycemia outcomes. Ideally, education should be provided through a diabetes self-management program or by a trained educator, although these services may not be universally available. Without structured education, clinicians should educate at-risk individuals on hypoglycemia definitions, potential triggers

(such as fasting, delayed meals, physical activity, and illness), blood glucose monitoring, the importance of avoiding driving with hypoglycemia, step-by-step hypoglycemia treatment, and appropriate glucagon use. Empowering patients with this knowledge can significantly reduce the incidence and severity of hypoglycemic episodes.<sup>3</sup>

Blood glucose monitoring (BGM) and continuous glucose monitoring (CGM) are crucial tools for managing diabetes. The advent of diabetes technology has introduced automated insulin delivery (AID) systems, where CGM data inform algorithms to adjust insulin delivery. Connected insulin pens and diabetes self-management support software further enhance patient care.<sup>4</sup> CGM is particularly valuable for detecting and preventing hypoglycemia, especially in insulin-treated individuals, including those on multiple daily injections or continuous insulin infusion. Clinical trials have shown that CGM effectively reduces hypoglycemia rates by detecting asymptomatic episodes and identifying patterns and triggers.<sup>5</sup> Personal CGM and AID devices, such as insulin pumps with real-time adjustment capabilities, should be encouraged for hospital use, provided patients can safely and independently operate them under proper supervision. This technology facilitates precise insulin delivery, improving glycemic control during hospitalization.<sup>2</sup> A randomized controlled trial investigates the efficacy of real-time continuous glucose monitoring (RT-CGM) systems in reducing inpatient hypoglycemia among high-risk patients with type 2 diabetes. The interim analysis reveals a significant decrease in hypoglycemic events with RT-CGM/GTS intervention, showing a relative risk reduction of 60.4%. Notably, there were no episodes of prolonged hypoglycemia in the RT-CGM/GTS group. Although the study did not find a reduction in nocturnal hypoglycemia, the use of RT-CGM/GTS holds promise in modifying institutional hypoglycemia prevention protocols, potentially reducing hospital charges and readmissions.<sup>14</sup>

Healthcare professionals advise individuals with diabetes to promptly treat hypoglycemia with fast-acting carbohydrates when blood glucose drops to 70 mg/dL or below. They should consume 15 g of carbohydrates and recheck their glucose levels after 15 minutes. If hypoglycemia persists, additional carbohydrates should be ingested, and medical attention sought. Glucagon is recommended for those unable to consume carbohydrates orally, with healthcare providers ensuring its availability and educating caregivers on its use. Ready-to-inject glucagon formulations are preferred for their ease of use and rapid effectiveness. Proper storage and replacement are crucial for safety and efficacy. Healthcare providers should consider insurance coverage and prescribe formulary products whenever possible.<sup>3</sup>

### Pharmacist role in inpatient hypoglycemia

In the hospital setting, pharmacists play a pivotal role in reducing hypoglycemia risk through the implementation of tailored glycemic control protocols, as evidenced by a pharmacist-led initiative resulting in a significant reduction in severe hypoglycemia events among high-risk diabetes patients over 4 years. Led by a Certified Diabetes Educator Pharmacist, the protocol identified at-risk patients and effectively managed their blood glucose levels according to established criteria. Physician acceptance rates were high,



ranging from 77% to 81%. The protocol resulted in a 74% relative reduction in severe hypoglycemic events, with a 15% decrease yearly. This collaborative approach improved diabetes care, strengthened physician-pharmacist relationships, and proved cost-effective, demonstrating the potential for similar protocols to enhance patient safety and quality of care in hospitals nationwide.<sup>15</sup> Hospital pharmacists are integral in preventing and managing blood sugar fluctuations. They ensure accurate medication histories, manage formularies, and recommend effective glycemic management strategies. To prevent hypoglycemia, they identify risk factors and adjust medications accordingly. After a hypoglycemia episode, pharmacists recommend reducing or discontinuing noninsulin glucose-lowering medications and/or insulin doses to prevent recurrence. It's essential to underscore that basal insulin should never be stopped in patients with type 1 diabetes mellitus or ketosis-prone type 2 diabetes mellitus.<sup>16</sup> Another study revealed that, Pharmacist intervention significantly improved blood glucose levels and minimized fluctuations, encompassing FBG, PBG, and overall BG, as well as SDBG, PBGE, and LAGE. Clinical pharmacists potentially mitigate hypoglycemia risk and enhance blood glucose control for diabetic AMI patients. A coordinated treatment model involving pharmacists and clinicians may offer substantial benefits in managing blood glucose, especially for those with cardiovascular complications.<sup>17</sup> In a retrospective observational study at a 502-bed teaching acute care community hospital in South Florida, pharmacists reviewed hypoglycemic alerts via an automated system in the electronic health record. This initiative resulted in a significant decrease in the percentage of recurrent hypoglycemia days during hospitalization. Specifically, out of 952 patient encounters pre-implementation and 1169 post-implementation, the pharmacist-led intervention led to a notable reduction in recurrent hypoglycemia days. The findings underscore the value of pharmacist involvement in hypoglycemia stewardship within hospital settings, showcasing the impact of collaborative efforts on patient safety and outcomes.<sup>18</sup> Pharmacists play a crucial role in diabetes management by contributing to rational drug selection for diabetes and associated conditions. They enhance patient awareness of hypoglycemia and educate them on recognizing and managing it early. Pharmacists also guide medication timing relative to meals, develop protocols for preventing and treating hypoglycemia, and tailor prevention strategies for at-risk patients. They assist in recognizing critical points during IV insulin therapy and recommend alternatives to insulin secretagogues for high-risk patients. Additionally, pharmacists ensure access to glucagon kits for severe hypoglycemia and optimize insulin and non-insulin therapies to minimize hypoglycemic risk while achieving glycemic targets. They may also advise on relaxed glycemic goals when necessary and direct patients to relevant educational resources and support groups for further assistance.<sup>5</sup>

## CONCLUSION

Inpatient hypoglycemia poses significant risks, including increased morbidity, longer hospital stays, and higher readmission rates, particularly among insulin-treated patients.

Preventive measures involve assessing risk factors, structured patient education, and utilizing advanced technologies like continuous glucose monitoring. Pharmacists play a crucial role in reducing hypoglycemia risk through tailored glycemic control protocols, medication management, and patient education. Collaborative efforts between healthcare professionals are essential for addressing the multifaceted factors contributing to hypoglycemia in hospital settings, ultimately enhancing patient safety and outcomes.

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