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Awareness and Management of Hypoglycemia among Adult Patients with Diabetes Mellitus: A Narrative Review

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Abstract **Review Article**

Hypoglycemia is a frequent and sometimes life-threatening complication of diabetes therapy, especially with insulin and insulin secretagogues. In primary care the prevention, early recognition, and prompt treatment of hypoglycemia are fundamental to safe, person-centered care. This narrative review synthesizes current global and regional evidence on the epidemiology, mechanisms, clinical manifestations, awareness, and management of hypoglycemia, with a particular lens on primary health care and recent data from Saudi Arabia and the Middle East and North Africa. We summarize contemporary definitions and thresholds, outline the pathophysiology of impaired counter regulation and impaired awareness of hypoglycemia (IAH), and highlight the clinical and psychosocial burden, including fear of hypoglycemia and its downstream effects on adherence, quality of life, and health care use. Evidence from multinational and regional studies shows that hypoglycemia nocturnal and daytime, mild and severe remains common across insulin-treated type 1 and type 2 diabetes, while patient awareness and first-aid practices are highly variable and often suboptimal. Determinants of low awareness include longer diabetes duration, older age, intensive insulin therapy, comorbidity, and inconsistent structured education. We translate guideline recommendations into brief, actionable steps that primary care teams can implement within routine visits: systematic screening for IAH, the 15–15 rule and rescue glucagon, individualized targets and de-intensification after level 2–3 events, and the strategic use of continuous glucose monitoring. We conclude with practice priorities and research gaps for primary care in Saudi Arabia, including culturally tailored education and digital support to strengthen self-management and reduce preventable hypoglycemia.

Keywords: Hypoglycemia; diabetes; impaired awareness; primary care; Saudi Arabia; continuous glucose monitoring.

INTRODUCTION

Diabetes mellitus is one of the most pressing chronic conditions in primary care. The International Diabetes Federation (IDF) estimates that approximately 589 million adults were living with diabetes in 2024, with projections reaching 853 million by 2050. The Middle East and North Africa (MENA) region continues to show among the steepest increases in prevalence and related mortality and spending. Within this context, hypoglycemia remains a critical safety concern and a major barrier to achieving durable glycemic control. Primary care teams, who deliver the majority of ongoing diabetes management, must balance individualized glycemic goals with the prevention of hypoglycemia and its consequences. (International Diabetes Federation, 2025)

Definitions, Classification, and Clinical Significance

Hypoglycemia in diabetes is commonly operationalized as a plasma glucose level below 70 mg/dL (3.9 mmol/L), a neuroendocrine threshold associated with activation of counter-regulatory responses. Authoritative statements from the American Diabetes Association (ADA) and a joint ADA/Endocrine Society workgroup also emphasize graded levels to guide risk communication and therapeutic action: level 1 (glucose <70 mg/dL and ≥54 mg/dL), level 2 (glucose <54 mg/dL), and level 3 (a severe event characterized by altered mental and/or physical status requiring assistance). These constructs standardize reporting across clinical practice and research and anchor primary care decision-making after an event. Importantly, iatrogenic hypoglycemia is not benign; it is associated with accidents and injuries, arrhythmias, reduced quality of life, and, in observational cohorts, higher all-cause mortality risk, particularly when episodes are severe or

recurrent. (Workgroup on Hypoglycemia, 2005; Seaquist ER *et al*., 2013; Zaccardi F *et al*., 2020)

Epidemiology and Burden in Primary Care and the MENA Region

International observational data confirm that hypoglycemic events are common among insulin-treated adults with type 1 and type 2 diabetes. In the multinational Hypoglycaemia Assessment Tool (HAT) program including 24 countries prospective 4-week diaries captured substantially higher rates than retrospective recall, underscoring under-reporting in routine care. Sub-analyses and regional reports from the Eastern Mediterranean show high frequencies of nocturnal and severe events, with fear of hypoglycemia independently associated with higher event rates. In Saudi Arabia, recent studies from different regions report high proportions of patients experiencing hypoglycemia or impaired awareness, including among those followed in primary care. In Aseer, only about one in eight adults with type 2 diabetes demonstrated good awareness of hypoglycemic episodes; in Al-Qassim, more than half of respondents screened positive for impaired awareness using Clarke or Gold instruments. During Ramadan in Abha, more than half of patients reported at least one episode. These findings highlight persistent gaps in recognition and self-management skills at the community level. (Khunti K *et al*., 2018; Amm M *et al*., 2020; Alqahtani F *et al*., 2024; AlTowayan A *et al*., 2023; AlKhaldi YM *et al*., 2019)

Pathophysiology: Counter-regulation, Recurrent Hypoglycemia, and Impaired Awareness

In health, falling glucose triggers a hierarchy of defenses: suppression of endogenous insulin, release of glucagon, and activation of the sympathoadrenal system chiefly epinephrine followed by autonomic (adrenergic/cholinergic) symptoms that cue carbohydrate intake. In insulin-deficient diabetes, the first two defenses are blunted: exogenous insulin cannot be down-regulated, and the glucagon response is often impaired; with repeated hypoglycemia, the sympathoadrenal response shifts to a lower glycemic threshold and becomes attenuated hypoglycemia-associated autonomic failure (HAAF). Clinically, this manifests as impaired awareness of hypoglycemia (IAH), where early autonomic warning symptoms are diminished and neuroglycopenia (confusion, behavioral change, seizures, coma) emerges abruptly. Short-term strict avoidance of hypoglycemia can restore awareness in many patients, underscoring the importance of identifying IAH and de-intensifying therapy after severe events. (Cryer PE, 2016; Workgroup on Hypoglycemia, 2005; Seaquist ER *et al*., 2013)

Clinical Manifestations and Psychosocial Impact

Symptoms of hypoglycemia range from autonomic (sweating, tremor, palpitations, hunger, anxiety) to neuroglycopenic (confusion, blurred vision, irritability, incoordination), with heterogeneity across individuals and over time. Beyond the immediate clinical risks, psychological sequelae are substantial. Fear of hypoglycemia (FoH) is common and can drive maladaptive behaviors, including defensive eating, intentional under-dosing or omission of insulin, and reluctance to titrate therapy; these behaviors worsen glycemic control, amplify variability, and reduce quality of life. Systematic and narrative reviews link FoH to prior severe episodes and to broader anxiety; structured education, diabetes technologies, and cognitive-behavioral strategies can mitigate FoH. (Frier BM, 2014; Anderbro T *et al*., 2015)

Determinants of Awareness and at-Risk Populations in Primary Care

In routine practice, lower awareness and higher hypoglycemia risk cluster with longer diabetes duration, intensive insulin regimens, chronic kidney disease, older age, polypharmacy, recent hospitalization, and a history of severe hypoglycemia. Primary care studies in Saudi Arabia add contextual drivers: variable health literacy, inconsistent reinforcement of self-management skills, and sociocultural patterns that affect meal timing (e.g., Ramadan fasting) and physical activity. Screening for IAH using brief tools (e.g., Clarke, Gold, or single-item prompts) is feasible in primary care and identifies patients who benefit from de-intensification, technology support, and targeted education. (Seaquist ER *et al*., 2013; AlTowayan A *et al*., 2023; AlKhaldi YM *et al*., 2019)

Immediate Management and Prevention: Translating Guidelines for Primary Care

Contemporary standards recommend that all individuals at risk for hypoglycemia be routinely asked about events at each encounter, screened for IAH, and educated on immediate treatment and prevention. Core elements include: (1) the 15–15 rule for conscious patients consume 15 g of fast-acting carbohydrate (e.g., glucose tablets, juice), recheck in 15 minutes, and repeat as needed until glucose is ≥70 mg/dL; (2) prescribe ready-to-use glucagon (nasal or autoinjector/pre-mixed) for anyone on insulin or with recurrent level 2–3 events; train family/caregivers; (3) review timing and doses of insulin and sulfonylureas relative to meals, activity, and alcohol; (4) individualize glycemic targets and de-intensify or switch therapies following level 2–3 hypoglycemia; and (5) deploy continuous glucose monitoring (CGM) or structured capillary monitoring to identify patterns, especially nocturnal hypoglycemia. These steps are feasible within brief primary care visits and align with patient-safety priorities. (ADA Standards of Care, 2025)

Structured Education, Digital Support, and Team-Based Care

Structured diabetes self-management education and support (DSMES) improves hypoglycemia knowledge, reduces events, and builds self-efficacy. Technology-enabled DSMES mobile apps, secure

messaging, remote monitoring can extend reach between visits and has been associated with clinically meaningful A1c reductions when interventions incorporate two-way communication, analysis of patient-generated data, tailored education, and individualized feedback. Within primary care, embedding brief hypoglycemia counseling scripts, standard orders, and referral pathways to educators or pharmacists strengthens consistency. (Greenwood DA *et al*., 2017)

Saudi Arabia and the MENA Region: Contextual Considerations

Saudi Arabia faces a high and rising diabetes burden. Regional data point to substantial rates of hypoglycemia among insulin-treated adults and variable awareness across communities. Primary care pathways should address culturally specific scenarios (e.g., fasting during Ramadan), integrate locally available glucagon formulations, and leverage national clinical practice guidance. Health system investments in DSMES capacity, CGM access for those at high risk, and pragmatic audit-and-feedback cycles can close safety gaps. (International Diabetes Federation, 2025; AlKhaldi YM *et al*., 2019)

A Practical Primary-Care Toolkit (Checklists)

- Ask at every visit: Any lows (<70 mg/dL) since last visit? Any need for assistance (level 3)? Any nocturnal events?
- Screen for impaired awareness: quick prompt (e.g., 'Do you feel symptoms when glucose is low?') or Clarke/Gold if time allows.
- Reconcile therapy: timing of insulin/secretagogues vs. meals, activity, alcohol; consider de-intensification after level 2–3 events.
- Educate (2–3 minutes): early symptoms; 15–15 rule; carry glucose; medic alert; driving safety; exercise adjustments.
- Prescribe and teach glucagon for those on insulin or at high risk; ensure caregivers know where it is and how to use it.
- Consider CGM or structured SMBG profiles to detect nocturnal and asymptomatic episodes; review reports together.
- Document and plan: set a shared hypoglycemia-prevention goal; schedule follow-up; refer to DSMES if available.

Future Directions and Research Gaps

Key unanswered questions in primary care include how best to operationalize routine IAH screening at scale; which combinations of education, digital support, and technology yield the greatest reduction in severe events; and how to tailor strategies for older adults and those with multimorbidity. Regionally, high-quality longitudinal studies from Saudi Arabia are needed to quantify hypoglycemia incidence across care settings, characterize FoH, and evaluate Ramadan-focused interventions. Pragmatic trials embedded in primary care that test brief counseling scripts, clinician prompts, and CGM-supported care could rapidly inform policy and practice.

CONCLUSION

Hypoglycemia remains common and consequential among people with diabetes, especially those treated with insulin, and it is frequently under-recognized in primary care. Evidence from global and Saudi studies demonstrates gaps in symptom recognition, first-aid management, and preventive behaviors, alongside substantial psychosocial burden. Primary care teams can meaningfully reduce risk with systematic screening for impaired awareness, brief structured education at every visit, judicious de-intensification after significant events, ready access to glucagon, and the targeted use of CGM. With culturally tailored DSMES and team-based workflows, primary care can improve safety, quality of life, and glycemic outcomes while advancing equitable diabetes care.

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