

Hypoglycemia, Chronic Kidney Disease, and Diabetes Mellitus

Mazen Alsahli, MD, and John E. Gerich, MD

Abstract

Hypoglycemia is a major problem associated with substantial morbidity and mortality in patients with diabetes and is often a major barrier to achieving optimal glycemic control. Chronic kidney disease not only is an independent risk factor for hypoglycemia but also augments the risk of hypoglycemia that is already present in people with diabetes. This article summarizes our current knowledge of the epidemiology, pathogenesis, and morbidity of hypoglycemia in patients with diabetes and chronic kidney disease and reviews therapeutic considerations in this situation. PubMed and MEDLINE were searched for literature published in English from January 1989 to May 2014 for *diabetes mellitus*, *hypoglycemia*, *chronic kidney disease*, and *chronic renal insufficiency*.

© 2014 Mayo Foundation for Medical Education and Research ■ Mayo Clin Proc. 2014;89(11):1564-1571

From the Faculty of Medicine, Department of Medicine, University of Toronto, Toronto, Ontario, Canada (M.A.); and Department of Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY (J.E.G.).

Hypoglycemia commonly occurs in people with diabetes, most frequently as a result of pharmacologic intervention. It is a major barrier to achieving optimal glycemic control¹ and can cause considerable morbidity and mortality.²⁻⁶

Chronic kidney disease (CKD) is an independent risk factor for hypoglycemia and augments the risk of hypoglycemic events already present in people with diabetes.⁷⁻⁹ In addition, CKD imposes restrictions on therapeutic options and increases the risk of cardiovascular disease and death.^{7,10-13}

To review this subject, PubMed and MEDLINE were searched for literature published in English from 1989 to May 2014 for *diabetes mellitus*, *hypoglycemia*, *chronic kidney disease*, and *chronic renal insufficiency*.

DEFINITION AND CLASSIFICATION OF HYPOLYCEMIA IN PATIENTS WITH DIABETES

The American Diabetes Association and the Endocrine Society workgroup on hypoglycemia defined *iatrogenic hypoglycemia* in patients with diabetes as all episodes of an abnormally low plasma glucose concentration that expose the patient to potential harm.¹⁴ No single threshold value was assigned to define hypoglycemia because this value may differ between patients. An alert value of less than 70 mg/dL (<3.8 mmol/L) was, however, chosen to be used to draw the attention of patients and caregivers and also as a cutoff value in

the classification of hypoglycemia in patients with diabetes as outlined in [Table 1](#).¹⁴

DEFINITION AND CLASSIFICATION OF CKD

The international guideline group Kidney Disease Improving Global Outcomes has defined CKD as abnormalities of kidney structure or function, present for more than 3 months, with implications for health.¹⁵ The group classified CKD on the basis of cause, glomerular filtration rate (GFR) category, and albuminuria category. Diabetic kidney disease (DKD) refers to CKD caused by diabetes. Diabetic kidney disease is usually a presumptive diagnosis detected clinically by screening for increased albuminuria and decreased GFR. Infrequently, kidney biopsies are needed to establish the diagnosis.¹⁵

Increased urinary protein excretion or albuminuria is usually detected by abnormal reagent strip urinalysis for total protein or by positive urine albumin-to-creatinine ratio (ACR) test. Although the appearance of increased albuminuria is usually the earliest finding of DKD, the severity of albuminuria does not necessarily predict DKD progression in patients with either type 1 or type 2 diabetes.¹⁶⁻¹⁸ The normal ACR in young adults is less than 10 mg/g (<1 mg/mmol).¹⁵ Tests that give abnormal results should be repeated at least twice over a 3- to 6-month period because of the large number of false positives.¹⁹ An elevated ACR can be confirmed by urine albumin excretion rate in a

timed urine collection, as necessary. Albuminuria categories in CKD are summarized in Table 2.

Estimating the GFR from serum creatinine is appropriate for staging and tracking the progression of CKD in most clinical situations, including in patients with DKD. The 2009 Chronic Kidney Disease Epidemiology Collaboration equation and its modifications are currently adopted by many clinical laboratories and were generally found more accurate than the Modification of Diet in Renal Disease Study equation and its modifications.^{15,20,21} Using the 2009 Chronic Kidney Disease Epidemiology Collaboration equation is therefore recommended by the Kidney Disease Improving Global Outcomes over the Modification of Diet in Renal Disease Study equation for estimating the GFR.¹⁵ Glomerular filtration rate categories are outlined in Table 3.

EPIDEMIOLOGY

The US National Health and Nutrition Examination Survey found that 19.3% of participants with diabetes (type 1 or 2) had an estimated glomerular filtration rate (eGFR) of less than 60 mL/min per 1.73 m².²² The prevalence of kidney disease, characterized by either reduced kidney function (eGFR of <60 mL/min per 1.73 m²) or albuminuria (ACR ≥3 mg/mmol [≥30 mg/g]), was approximately 50% in patients with diabetes.²² The prevalence appears

ARTICLE HIGHLIGHTS

- Treatment with insulin or insulin secretagogues and impaired hypoglycemia counterregulation are the main causes of hypoglycemia in patients with diabetes.
- Chronic kidney disease (CKD) is an independent risk factor for hypoglycemia and augments the risk of hypoglycemic events already present in people with diabetes.
- Both hypoglycemia and CKD are associated with increased morbidity and mortality, particularly from cardiovascular disease.
- Presence of CKD limits therapeutic options in patients with diabetes.
- Judicious management of antidiabetic regimens is crucial to reduce the risk of hypoglycemia in patients with diabetes.

to be similar in several other countries. In the United Kingdom, one study found that patients with diabetes (type 1 or 2) were 7 times more likely to have clinically substantial CKD (defined as an eGFR of <60 mL/min per 1.73 m²) than those without diabetes. Almost one-third of people with diabetes (28.9%) had an eGFR of less than 60 mL/min per 1.73 m² as compared with only 6.7% of the general population.²³ In 2011, diabetes was the primary cause of new cases of end-stage renal disease (ESRD) in 59% to 61% of patients in Malaysia, Mexico, and Singapore. The Republic of Korea,

TABLE 1. Hypoglycemia Categories as Defined by the American Diabetes Association and the Endocrine Society

Category	Definition
Documented symptomatic	An event during which typical symptoms of hypoglycemia are accompanied by a measured plasma glucose concentration of ≤70 mg/dL ^a
Severe	An event requiring assistance of another person to administer carbohydrate, glucagon, or other resuscitative actions ^b
Asymptomatic	An event not accompanied by typical symptoms of hypoglycemia but by a measured plasma glucose concentration of ≤70 mg/dL ^a
Probable symptomatic	An event during which symptoms of hypoglycemia are not accompanied by a plasma glucose measurement but that was presumably caused by a plasma glucose concentration of ≤70 mg/dL ^a
Pseudohypoglycemia	An event during which the person with diabetes reports any of the typical symptoms of hypoglycemia accompanied by a measured plasma glucose concentration of >70 mg/dL ^a but approaching that level

^a70 mg/dL equals 3.8 mmol/L.

^bIf plasma glucose measurements are not available during such an event, the neurological recovery attributable to the restoration of plasma glucose to the normal level is considered sufficient evidence that the event was induced by hypoglycemia.

Data from *Diabetes Care*.¹⁴

Download English Version:

<https://daneshyari.com/en/article/10165637>

Download Persian Version:

<https://daneshyari.com/article/10165637>

[Daneshyari.com](https://daneshyari.com)