

Prediabetes

A Worldwide Epidemic

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KEYWORDS

- Prediabetes • Impaired glucose tolerance • Impaired fasting glucose
- Type 2 diabetes • Metabolic syndrome • β -Cell • Insulin resistance

KEY POINTS

- Prediabetes is increasing markedly in incidence and prevalence, particularly in Africa and Asia.
- The central reason for this epidemic is increased calorie-dense food and decreased physical activity.
- Prediabetes carries significant risk for both macrovascular and microvascular disease.
- Prospective studies have demonstrated the potential to prevent or delay the onset of type 2 diabetes mellitus in patients with prediabetes with lifestyle changes and pharmacologic therapy.

DEFINITION AND THE DIAGNOSIS OF PREDIABETES

Prediabetes is the state between normal and diabetes; its definition has evolved over time and still varies depending on the defining institution (**Table 1**). It generally reflects the presence of either, or both, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT).^{1,2} The American Diabetes Association (ADA) also includes the A1c as a diagnostic criterion. Various terms have been used to refer to this metabolic state, in addition to prediabetes, IFG, and IGT; intermediate hyperglycemia is preferred by the World Health Organization (WHO), and an expert committee convened by the ADA has suggested high-risk state of developing diabetes. The reproducibility of

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| Institution/Year of Publication | Venous Plasma Glucose |
|--|--|
| WHO, 2006 | IFG: 110–125 mg/dL (6.1–6.9 mmol/L) IGT: 140–200 mg/dL (7.8–11.0 mmol/L) 2 h after a 75 g oral glucose challenge |
| ADA, 2016 | IFG: 100–125 mg/dL (5.5–6.9 mmol/L) IGT: 140–200 mg/dL (7.8–11.0 mmol/L) 2 h after a 75 g oral glucose challenge A1c: 5.7% to 6.4% |

the definition of prediabetes (50%) is less than that of diabetes (>70%).³ The variations in defining threshold glucose levels and this low reproducibility of the tests themselves result in variability in populations of patients defined as having prediabetes in clinical studies.

Prediabetes is clearly the major risk factor for the future development of type 2 diabetes mellitus (T2DM). In addition, other risk factors, like family history of T2DM, or a personal history of gestational diabetes, polycystic ovary syndrome (PCOS), nonalcoholic fatty liver disease (NAFLD), obesity, or metabolic syndrome (MS), can markedly increase the risk of developing T2DM. Various biomarkers have been examined and risk scores developed in an effort to improve the ability to predict the progression of prediabetes to T2DM, but these have not yet achieved frequent clinical use.⁴ In addition, there are important ethnic differences in the risk of developing diabetes, perhaps necessitating different algorithms depending on ethnicity.⁵

EPIDEMIOLOGY

The incidence and prevalence of prediabetes is increasing in both developed and developing countries. The Centers for Disease Control and Prevention (CDC) estimated that 37% of adults in the United States over the age of 20, and 51% of those over 65, had prediabetes in the period 2009 to 2012, as determined by fasting glucose or A1c.⁶ The International Diabetes Federation (IDF) estimated the worldwide prevalence of IGT at 280 million in 2011 with projections of 398 million by 2030.⁷ Emphasizing the risk of progression of prediabetes to diabetes, the recent 2016 WHO Global Report on Diabetes⁸ reports that in 2014, 422 million adults had diabetes. This increase has been particularly marked in African and Asian countries.⁸

The chronicity of the disease and the high cost of care make these predictions an issue of great concern, and necessitate estimates of the financial burden for future policy making and planning. A review by Lam and LeRoith in 2012⁹ summarized evidence that rapid urbanization has altered diet, with increased intake of vegetable fat and increased glycemic load and index. The rapid changes in urbanization and diet in developing countries have thus likely resulted in an accelerated increase in average body mass index (BMI) and prediabetes. Lam and LeRoith⁹ also stress that genetic differences in different populations may play an important role in the global prediabetes and diabetes epidemic.

PATHOGENESIS OF PREDIABETES

Both resistance to the action of insulin and impaired β -cell function are present during even early stages of prediabetes and are required for most of the hyperglycemia seen

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