

# Prediabetes and Diagnosis: A Review

Alexandra Cruiser\*

Department of Nephrology, Stanford University, United States

## Prediabetes

Prediabetes is a state of intermediate hyperglycemia. While there are several controversies about the diagnosis of prediabetes, it remains an at-risk state for development of diabetes. Several adverse health outcomes have been associated with prediabetes. This review provides a detailed description of the current literature regarding diagnosis, health consequences and treatment of prediabetes and also provides an insight for clinical management.

## Diagnosis of Prediabetes

Various organizations have defined prediabetes with criteria that are not uniform. The World Health Organization (WHO) has defined prediabetes as a state of intermediate hyperglycaemia using two specific parameters, impaired fasting glucose (IFG) defined as fasting plasma glucose (FPG) of 6.1-6.9 mmol/L (110 to 125 mg/dL) and impaired glucose tolerance (IGT) defined as 2h plasma glucose of 7.8-11.0 mmol/L (140-200 mg/dL) after ingestion of 75 g of oral glucose load or a combination of the two based on a 2 h oral glucose tolerance test (OGTT) [1]. The American Diabetes Association (ADA) on the other hand has the same cut-off value for IGT (140-200 mg/dL) but has a lower cut-off value for IFG (100-125 mg/dL) and has additional haemoglobin A1c (HbA1c) based criteria of a level of 5.7% to 6.4% for the definition of prediabetes. Several studies have shown poor correlation between HbA1c and IFG and IGT. The usefulness of diagnosis of diabetes or prediabetes on basis of IFG and IGT have been challenged due to inability of these blood glucose cut points to capture pathology related to diabetes and probability of developing diabetes in future. These cut-offs further lose their credibility due to poor reproducibility of these tests in adults and children [2]. Although, HbA1c is believed to represent an average blood sugar level and should ideally represent hyperglycaemia more accurately, this may not be entirely true. HbA1c is substantially determined by genetic factors independent of blood glucose levels and may be an imprecise tool to measure average blood sugar. While there are valid concerns about diagnostic criteria of prediabetes, it remains to have a lower reproducibility (approximately 50%) than diabetes (approximately 70%) [3]. Based on the available evidence, it appears that prediabetes defined by various alternative criterions consists of an overlapping group of individuals with one or more abnormalities in their glucose excursions. It is possible that presence of IFG and IGT identifies subjects with different pathological abnormalities in their glucose metabolism and presence of both of these signifies more advanced impairment in overall glucose homeostasis.

## Prevalence of Prediabetes

There have been reports of increased mean FPG and prevalence of diabetes in developed as well as developing countries. The Centres of Disease Control and Prevention National Diabetes Statistics Report suggested that 37% of United States adults older than 20 years and 51% of those older than 65 had prediabetes in 2009-2012 defined by fasting glucose or HbA1c levels. When applied to the entire United States population in 2012, these estimates suggest that, there are nearly 86 million adults with prediabetes in United States alone [4]. The worldwide prevalence of IGT in 2010 was estimated to be 343 million (7.8%) ranging from 5.8% in South East Asia to 11.4% in

North American and Caribbean Countries of the nation's population. International Diabetes Federation projects an increase in prevalence of prediabetes to 471 million globally by 2035.

## Progression to diabetes

The conversion rate of individuals from prediabetes to diabetes changes with population characteristics and the criteria used to define prediabetes. In a meta-analysis evaluating the progression of prediabetes to diabetes published in 2007, the annual incidence rate of diabetes was found to be 4%-6% for isolated IGT, for isolated IFG 6%-9% and for both IGT and IFG was 15%-19%. This meta-analysis only consisted of studies published prior to 2004. In subsequently reported major studies, the annual incidence rates of conversion from prediabetes to diabetes were similar. In the Diabetes Prevention Program (DPP) Outcomes Study, the incidence of diabetes was noted to be 11% in the control group. In the United States Multi-Ethnic Study of Atherosclerosis the annual incidence of diabetes in IFG group slightly above 4%. In The Toranomon Hospital Health Management Center Study the incidence of diabetes was reported as 7% in the group with an HbA1c 5.7%-6.4% and 9% in the IFG group. In the China Da Qing Diabetes Prevention Study (CDQDPS), the cumulative incidence of diabetes over a 20 years period was noted to be higher than 90% among subjects with IGT defined by repeated OGTT in the control group [5]. The use of ADA vs WHO criteria to define prediabetes has also been shown to affect the incidence rate of diabetes with lower incidence in individuals defined by ADA criteria compared to WHO criteria.

According to an expert panel, continuous rather than dichotomous risk scores are more useful for predicting the risk of developing diabetes. A diabetes risk score based more easily accessible variable such as age, sex, ethnicity, fasting glucose, systolic blood pressure, HDL cholesterol, BMI and history of diabetes in parents or siblings has been shown to have better predictive value than either IFG or IGT.

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\*Corresponding author: Alexandra Cruiser, Department of Nephrology, Stanford University, United States, E-mail: alexandra@stanford.edu

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