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Diagnostic thresholds for diabetes: The association of retinopathy and albuminuria with glycaemia

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Abstract

Aim: We examined the association of fasting plasma glucose (FPG), 2-h plasma glucose (2hPG) and HbA1c with retinopathy and microalbuminuria using both deciles of glycaemia and change point models, to validate current diagnostic criteria for diabetes and to identify therapeutic thresholds for glycaemic control.

Methods: The Australian Diabetes Obesity and Lifestyle study (AusDiab), conducted in 1999–2000, included adults aged ≥25 years from 42 randomly selected areas of Australia. Retinopathy and albuminuria were assessed in participants identified as having diabetes (based on self report and oral glucose tolerance test), impaired fasting glucose, impaired glucose tolerance and in a random sample with normal glucose tolerance. Data were available for 2182 participants with retinal photographs and 2389 with urinary albumin/creatinine results.

Results: The prevalence of retinopathy in the first 8 deciles of FPG and HbA1c and the first 9 deciles of 2hPG were 7.2, 6.6, and 6.3%, respectively and showed no variation with increasing glucose or HbA1c. Above these levels, the prevalence rose markedly to 18.6% in the top 2 deciles of FPG, 21.3% in the top 2 deciles of HbA1c and 10.9% in the top decile of 2hPG. The thresholds for increasing prevalence of retinopathy were 7.1 mmol/l for FPG, 6.1% for HbA1c and 13.1 mmol/l for 2hPG. The prevalence of microalbuminuria rose gradually across deciles of each glycaemic measure. Thresholds were less clear than for retinopathy, but were seen at a FPG of 7.2 mmol/l and HbA1c of 6.1%, with no evidence of a threshold effect for 2hPG.

Conclusions: The prevalence of retinopathy rose dramatically in the highest deciles of each glycaemic measure, while for microalbuminuria the increase of prevalence was more gradual. The FPG values corresponded well with the WHO diagnostic cut-point for diabetes, however the 2hPG value did not. HbA1c thresholds were similar for both retinopathy and microalbuminuria and

Abbreviations: AusDiab, Australian diabetes, obesity and lifestyle study; FPG, fasting plasma glucose; HbA1c, glycated haemoglobin; KDM, known diabetes mellitus; NDM, newly diagnosed diabetes mellitus; NGT, normal glucose tolerance; OGTT, oral glucose tolerance test; TIFF, tagged image format files; 2hPG, 2-h post glucose load; WHO, World Health Organization

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compared well to values shown in other studies. These results support current targets for FPG and HbA1c in preventing microvascular complications.

Keywords: Diabetes mellitus; Diabetic retinopathy; Diagnostic criteria; Epidemiology

Continued improvement in our understanding of the aetiology and pathogenesis of diabetes mellitus has led to several modifications and improvements in the diagnostic criteria for diabetes. The most recent of these changes have been widely adopted throughout the world [1,2]. The diagnostic criteria for diabetes have been based on an assessment of several criteria. Early methods of diagnosing diabetes were based on clinical symptoms and the mean glycaemic value plus two standard deviations of blood glucose (among those without diabetes, or a family history of diabetes) [3]. Many limitations were identified with this approach and new methods of diagnosis were sought. Several studies were undertaken [4–10] and in 1979, these studies were evaluated and a report on the classification and diagnosis of diabetes mellitus was published [11].

The most recent report released in 1999 made several modifications to the diagnostic criteria using results from studies assessing bimodal distributions and thresholds for microvascular complications [12]. Bimodal distributions of blood glucose were identified in populations with very high prevalences of diabetes [9,13]. In these populations, two overlapping distributions of normal and high blood glucose levels provided a better model, than one uni-model distribution (those in the high part of the distribution were classified as having diabetes) [14–17]. The diagnostic values identified using this technique were later shown to fit well with those identified by assessing population thresholds for microvascular complications [15]. The use of microvascular end points (retinopathy and microalbuminuria) to define glycaemic thresholds for diabetes was an important step in the development of the current diagnostic criteria, as those at high risk of developing diabetes related complications were identified. Thresholds using this approach were identified from population-based cohorts, including those with and without diabetes, by constructing deciles of glycaemia (fasting plasma glucose (FPG) and 2-h plasma glucose (2hPG)) and taking the lower limit of the decile in which the prevalence of complications markedly increased, as the threshold for diabetes.

Despite the current diagnostic criteria for diabetes being largely based on the association of glycaemia with microvascular complications, few published studies have assessed this association [18–21]. Of the few studies that have been published, all have had a relatively small number of cases and no population-based study has used the full spectrum of glucose values and assessed the association of microvascular complications with glycaemia in a continuous form**.** We examined the association of fasting plasma glucose (FPG), 2-h plasma glucose (2hPG) and HbA1c with retinopathy and microalbuminuria using both deciles and change point models, to validate current diagnostic criteria for diabetes and to identify therapeutic thresholds for glycaemic control.

1. Methods

1.1. Sample selection

The Australian Diabetes, Obesity and Lifestyle study (AusDiab) was a population-based study of 11,247 people age ≥25 years from 42 randomly selected urban and rural areas of Australia [22]. A stratified cluster sampling method was used, involving seven strata (six states and the Northern Territory) and clusters were based on census collector districts. Of those who completed the initial household interview 55.3% attended the biomedical examination. Participants not on current treatment for diabetes (insulin or tablets) underwent an oral glucose tolerance test (OGTT). Diabetes classification was based on plasma glucose results, using the 1999 World Health Organization (WHO) diabetes classification [1].

Participants identified through the AusDiab study as having diabetes (both known and newly diagnosed), impaired glucose tolerance, impaired fasting glucose and a random sample of those with normal glucose tolerance were eligible to attend the complications study ($n = 2773$). Participants with NGT were selected using a systematic random sample selecting every nth person. The value of n was dependant upon the number of people expected on each day of testing, in order to obtain a sample size of 10 per day. Of 2773 participants eligible to attend the complications component, 2476 attended (overall response rate 89%, 91% in those with diabetes and 88% in those without diabetes). There were 431 people with KDM, 424 with NDM, 1155 with IGT or IFG and 466 with NGT. After exclusion of participants who were unable to be photographed or whose photographs were not gradable or who did not have pathology results for microalbuminuria, data were available for 2182 participants for the retinopathy study and 2389 for the microalbuminuria study. There was no