

Opinion

Geographic and Ethnographic Variations of Hemoglobin A1C

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Around the world, approximately 9% of adults are currently living with type 2 diabetes mellitus (T2DM).¹ In the United States, 50% of the population may suffer from undiagnosed diabetes, and in other countries, the percentage could be higher. For this reason, it is important to establish worldwide criteria for detecting diabetes or prediabetes in asymptomatic adults.²

In 2010, the American Diabetes Association (ADA) recommended the use of HbA1c (A1C) for the diagnosis of type 2 diabetes.² This was based on the results of a test with a limit or cut-off point of $\geq 6.5\%$ (48 mmol/mol).³ This limit was strongly related to retinopathy. The ADA has recently published standards for classification and diagnosis of diabetes, which broaden the range of its categorization to include prediabetes with A1C levels ranging from 5.7% to 6.4% (39–47 mmol/mol).⁴

However, significant variations in geographical prevalence, ethnic group, age, and gender make us reconsider the criteria carefully. Other research which debates the previous assertions has been reported.⁵ There are already several known studies of diabetes with differences in geographical data, for example, in a systematic review by Bennett et al, for diagnosis of type 2 diabetes, the A1C had a cut-off point of $\geq 6.1\%$,⁵ sensitivity varied from 78 to 81% and specificity was 79 to 84%.⁵ Two groups of patients were selected; the first from community-based studies, and the second from hospital-based studies. The results are as follows: Colagiuri, Australia, 2004 (cut-off point $\geq 5.3\%$); Mannucci, Italy, 2003, (cut-off point $>6.6\%$); Saydan, USA, 2002, (cut-off point $>6.0\%$); Wiener, UK, 1998, (cut-off point $>6.9\%$); Adelaide, Australia, 2003 (cut-off point $\geq 4.7\%$); Herdzyk,

Poland, 2002 (cut-off point $\geq 6.4\%$); Tanaka, Japan, 2001 (cut-off point $\geq 5.9\%$); Tavintharan, Singapore, 2000 (cut-off point $\geq 5.9\%$); and Ko, Hong Kong, 1998 (cut-off point $\geq 6.1\%$).

An additional study in Melbourne, Australia, by Lu et al, in 2010, found a cut-off point $\leq 5.5\%$ for A1C, which predicted an absence of type 2 diabetes, whereas $\geq 7.0\%$ predicted its presence, and an A1C between 6.5 and 6.9% predicted a high type 2 diabetes prevalence.⁶

In a selected Spanish population, Costa et al⁷, when A1C was used as the main diagnostic criterion, the detection of diabetes decreased to 5.6%–20.3%. For populations in southern and northern India, the optimal A1C cut-off point for type 2 diabetes was 5.8%, with a sensitivity of 75% and a specificity of 75.4%. However, for prediabetes/IFG (impaired fasting glucose, ADA criteria), the cut-off point of 5.5% had an optimum sensitivity of 59.7% and specificity of 59.9%.⁸

An interesting study by Hellgren et al,⁹ compared two groups of ancestors, Middle-Eastern (Iraq, Turkey) and Swedish, and showed a very low A1C sensitivity in detecting T2DM or prediabetes. Other studies show that the sensitivity and specificity of A1C is very variable in different populations, which prevents the recommendation of an international cut-off point (Table 1). A research by Tuomilehto,¹⁰ on the "expert-opinion-based consensus recommendations", states that the criteria is not necessarily helpful in clinical practice. We think that the recommendations need to be more specific to the geographic and ethnographic populations and individual cases.

Table 1. Different Geographical Reports With Cut-off Point Variations

	Type 2 Diabetes Mellitus			Prediabetes (IFG or IGT)		
	Cut-off Point %	Sensitivity %	Specificity %	Cut-Off Point %	Sensitivity	Specificity
San Diego, La Jolla, California ¹¹	6.5	44	79			
Shanghai, China ¹²	6.1	81.5	81.0	5.6	66.2	51.0
Chandigarh, northern India ¹³	6.1	81.0	81.0			
India, southern and northern ⁹	5.8	75	75.4	5.5	59.7	59.9
Middle-East ancestry (Iraq, Turkey) ⁹	6.5	30.9	99.2	6.0	16.9	92.1
Swedish ancestry ⁹	6.0	25.2	99.9	6.0	15.2	92.7

Abbreviations: IGF, impaired fasting glucose; IGT, impaired glucose tolerance.

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Conflict of Interest Disclosures

None.

Ethical Statement

Not applicable.

Authors' Contribution

EPCM, LPCM contributed to the conception and design of the manuscript. GMA, MTHH, MMC and EPC contributed to data collection. EPC prepared, wrote and approved the final version of the manuscript.

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