

Prediabetes and intermediate hyperglycemia prevalence in adults and associated factors, Health National Survey

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Abstract *This study aimed to evaluate the prevalence of prediabetes and intermediate hyperglycemia in Brazilian adults, according to different diagnostic criteria, and establish associated factors to its occurrence. We analyzed the National Health Survey laboratory data collected from 2014 to 2015. The prevalence of the conditions was calculated according to the American Diabetes Association (ADA) diagnostic criteria based on glycated hemoglobin (HbA1c) 5.7%-6.4%, and the World Health Organization (WHO) 6-6.4%, among those without criteria for diabetes. Crude and adjusted prevalence rates (PR) and 95% CI were calculated using Poisson regression with robust variance. The prevalence of prediabetes by ADA and WHO criteria was 18.5 and 7.5%, respectively. We observed a gradient of increased prevalence by the age of the population and risk factors, like arterial hypertension, obesity, elevated waist circumference, and low HDL cholesterol levels. Less educated people and the self-declared black had a higher prevalence. This study pointed out a range from 7.5 to 18.5% of Brazilian adults with prediabetes and intermediate hyperglycemia and identified a risk score to this condition's occurrence.*

Key words *Hyperglycemia, Prediabetic state, Glycated Hemoglobin A, Epidemiological surveys, Risk factors*

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Introduction

Intermediate metabolic states characterized by high glycemic levels, above “normal”, show an increased risk for diabetes mellitus and its complications, including cardiovascular diseases¹. Five to ten percent of people with the intermediate condition is estimated to progress to type 2 diabetes mellitus². Zhang’s systematic review indicated that HbA1c values from 6 to 6.5% are associated with an incidence of 25 to 50% of DM within the next five years³.

On the other hand, as it is considered an intermediate condition, it is likely to stabilize in the face of a healthy lifestyle, such as food control, weight loss/maintenance, and regular physical activity. Thus, its early detection can identify high-risk individuals, eligible for stricter, preventive strategies, creating adequate control opportunities.

The American Diabetes Association (ADA) calls this condition ‘prediabetes’ and recommends its screening in asymptomatic individuals when associated risk factors, such as obesity, high blood pressure, and dyslipidemia¹, are found. The World Health Organization contraindicates the use of the term prediabetes, preferring ‘intermediate hyperglycemia’⁴.

Although the diagnostic criteria have been much debated in recent years, there is still no consensus on the limits to be considered for this intermediate stage, concerning increased complications, considering the cutoff points established for diabetes, of 7mmol/L or 126 mg/dL of fasting blood glucose, or 6.5% glycated hemoglobin (HbA1c), as shown in Chart 1^{1,4,5}.

Considering the diverging criteria and nomenclatures, the estimates of prediabetes/intermediate hyperglycemia prevalence are scarce. The

International Diabetes Federation (IDF), considering the levels of glucose intolerance proposed by the World Health Organization (WHO) – fasting blood glucose < 126 mg/dL and oral glucose tolerance test (OGTT) ≥ 140 and < 200 mg/dL – indicates more than 370 million people worldwide with this condition, representing a prevalence of 7.5%. More than 70% of these belong to low-middle income countries, and about 28% are in the 20-39 years’ age group. The estimated prevalence of Central and South America is 9.7%⁶.

The Brazilian Diabetes Society (SBD) adopts criteria similar to the ADA, where prediabetes is when the fasting blood glucose ranges from 100 to 126 mg/dL (altered fasting glucose) or impaired glucose tolerance with values ranging from 140 to 199 mg/dL (oral glucose intolerance) 2h after the oral glucose tolerance test (OGTT), or glycated hemoglobin (HbA1c) values from 5.7 to 6.4%⁷.

The HbA1c measure is accepted for the screening of prediabetes and diabetes by the ADA/SBD. While more convenient because it does not require fasting, it reflects a more stable value, referring to a previous period (8-12 weeks), and is independent of momentary variability. However, it is influenced by factors such as ethnicity, age, and hemoglobinopathies, with some limitations regarding its use in isolation⁸.

The adoption of different diagnostic criteria can be influenced by specific policies and affect people’s quality of life and health expenditure, which may burden public services. On the other hand, a less sensitive criterion may miss the opportunity to diagnose and treat disease-related complications early.

This study aimed to assess the prevalence of intermediate hyperglycemia and prediabetes in Brazilian adults, considering different diagnostic

Chart 1. Laboratory criteria and cutoff points for diagnosing prediabetes/intermediate hyperglycemia and diabetes, according to the proposing entity.

Criteria / Cutoff points	ADA / SBD	WHO / IDF / IEC	All
	Prediabetes	Intermediate Hyperglycemia	Diabetes
Fasting blood glucose	100-125 mg/dL* (5.6-6.9 mmol/L)	110-125 mg/dL (6.1-6.9 mmol/L)	126 mg/dL (< 7.0 mmol/L)
Oral glucose tolerance test (OGTT) 2h after 75g glucose overload	140–199 mg/dL (7.8–11.0 mmol/L)#	140 e 199 mg/dl (7.8–11.0 mmol/L)#	≥ 200 mg/dL (11.1 mmol/L)
Glycated hemoglobin (HbA1c)	5.7 – 6.4% (39-47 mmol/mol)	6 – 6.4% (42-47 mmol/mol)	≥ 6.5% (48 mmol/mol)

ADA: American Diabetes Association; SBD: Brazilian Diabetes Society; WHO: World Health Organization; IDF: International Diabetes Federation; IEC: International Expert Committee.

*Category known as altered fasting blood glucose. # Category known as impaired glucose intolerance.

criteria, and establish factors associated with its occurrence.

Methods

Laboratory data from the National Health Survey (PNS) from 2014 to 2015 were analyzed. PNS is a three-step nationwide household-based survey using probabilistic samples. The primary sampling units were census tracts or tract groups, secondary units, households, and tertiary units, and adult residents aged 18 years or over.

The interviews were conducted in 64,348 households, and 60,202 residents answered the individual questionnaire. Initially, 25% of the census tracts were selected to perform laboratory tests and, assuming a non-response rate of 20%, the expected number of individuals with laboratory data was approximately 12,000⁹. The subsample was selected with a probability proportional to the inverse of the distance from the municipality where the primary sampling unit is located and the closest municipality with 80 thousand inhabitants or more (relative to the difficulty of the collection) in all Federative Units. Considering the losses in the subsample of individuals indicated for laboratory tests, due to the difficulty in locating the address by the contracted laboratory or the refusal of the selected resident to perform the collection of biological material, tests were collected in 8,952 people. The weighting of the sampling process and post-stratification weighting were performed by gender, age, schooling, and region to adjust possible biases.

HbA1c was collected in a tube with ethylene diamine tetraacetic acid (EDTA) and dosed by ion-exchange-high-performance liquid chromatography (IEX-HPLC) in a laboratory certified by the National Glycohemoglobin Standardization Program (NGSP). Peripheral blood was collected at any time of the day without fasting¹⁰.

Concerning the analysis, the comparison of different diagnostic criteria was initially considered: the ADA's cutoff for prediabetes $5.7\% \geq \text{HbA1c} \leq 6.4\%$ ¹ and a narrower range accepted by the WHO for intermediate hyperglycemia: $6\% \geq \text{HbA1c} \leq 6.4\%$ ⁴. The prevalence of prediabetes and intermediate hyperglycemia was calculated among the respondents, excluding those with blood glucose $\geq 6.5\%$, who met the criteria for diabetes, regardless of having already been diagnosed with the disease, and individuals with missing information for the variables of inter-

est in the study, as described below. Prevalence was calculated according to sociodemographic characteristics: gender, age, schooling, ethnicity/skin color, the region of the country; Body Mass Index (BMI), categorized into eutrophic and low weight ($< 25 \text{ kg/m}^2$), overweight (between 25 and 29.9 kg/m^2) and obesity ($\geq 30 \text{ kg/m}^2$), and waist circumference, obtained in the midpoint between the lower border of the last rib and the upper border of the iliac crest, which can be considered an indicator of visceral fat. The measurement $\geq 102 \text{ cm}$ in men and 88 cm in women indicates cardiovascular risk and was considered in this study. The presence of other risk factors was also verified, such as arterial hypertension (defined by blood pressure ≥ 140 or 90 mmHg , by the report of medical diagnosis of arterial hypertension or use of antihypertensive medication), and low HDL cholesterol level, and $< 40 \text{ mg/dl}$ for men and $< 50 \text{ mg/dl}$ for women were considered cutoff points and measured in the same blood sample. Two behavioral risk factors were also considered: physical inactivity and low consumption of fruits and vegetables. Those who did not perform any leisure time physical activity in the last three months were considered inactive, and those who did not achieve at least 150 minutes of weekly physical activity considering leisure, work, and commuting, were insufficiently active. Low consumption of fruits and vegetables was identified in those who did not report eating these foods five times a day for at least five days a week. Furthermore, we calculated how much these recognized risk factors' simultaneous occurrence affects the prevalence of prediabetes/intermediate hyperglycemia.

The analyses were performed with the statistical program Data Analysis and Statistical Software (Stata), version 14, using the *survey* command to incorporate the post-stratification weightings. Bivariate analysis and prevalence calculations were performed, with a 95% confidence interval (95% CI).

Prevalence ratios (PR) were calculated using the Poisson regression method with robust variance, crude and adjusted by multivariate analysis, considering the other variables of interest. The number of risk factors in the same individual was considered for assessing by risk score, including increased waist circumference, obesity, hypertension, high cholesterol, physical inactivity, low consumption of fruits and vegetables, and age (≥ 60 years).

The National Research Ethics Commission (CONEP) approved the PNS. The research par-

ticipants signed the Informed Consent Form (ICF) and authorized the collection of laboratory tests.

Results

A total of 7,548 participants from 8,541 individuals with HbA1c analysis in the sample were considered in this study, as we excluded 595 respondents with a level of HbA1c compatible with diabetes ($\geq 6.5\%$, 310 with previous diagnosis report) and 398 more due to missing information.

The prevalence of prediabetes, considering ADA criteria, was 18.5% (95% CI 17.4-19.7), with no significant difference by gender. Under the criteria recommended by the WHO, the prevalence of intermediate hyperglycemia was more than twice as low, at 7.5% (95% CI 6.7-8.3), as detailed in Table 1. In both criteria, a gradient of increased prevalence by age is observed and is four times higher in older adults (≥ 60 years). On the other hand, the most educated had a lower prevalence of prediabetes/intermediate hyperglycemia than those with up to eight years of study.

Significant differences were observed in the adjusted analysis regarding ethnicity/skin color, with a higher prevalence for the self-declared black in both criteria. A lower prevalence for self-declared brown was verified only in crude analysis, under the ADA criterion. The Southeast had a higher prevalence among the Brazilian macro-regions in both criteria, and the Midwest, according to the ADA criterion.

Among the investigated morbidities, overweight, according to the ADA criterion, and obesity, according to both criteria, were factors related to the higher prevalence of prediabetes/intermediate hyperglycemia. Increased waist circumference, arterial hypertension, and low HDL cholesterol were associated with a higher prevalence of prediabetes/intermediate hyperglycemia. Physical inactivity was related to a higher prevalence of prediabetes/intermediate hyperglycemia than those considered active only in crude analyses. Although the prevalence of intermediate hyperglycemia has occasionally reduced in physically active adults according to the WHO criterion, the differences were not statistically significant in the adjusted analysis. Likewise, the consumption of fruits and vegetables was not related to the verified prevalence levels.

Table 2 shows the risk score, considering only the population with at least one factor ($n = 7,297$). It appears that, based on three incorpo-

rated risk factors, the prevalence of prediabetes/intermediate hyperglycemia increases, regardless of the diagnostic criterion used, although these differences are more pronounced with the WHO cutoff point. The presence of five or more risk factors increases the prevalence in a more significant proportion, with prevalence ratios up to four times higher than those with a risk factor.

Figure 1 shows the crude prevalence according to diagnostic criteria and independent variables. We can observe a higher prevalence from the ADA cutoff point. In contrast, for some variables, such as ethnicity/skin color and physical inactivity, higher inter-stratum differences are observed with the WHO criterion: between blacks and others, including yellow and indigenous, and between active and inactive.

Discussion

This study evidenced the prevalence and factors associated with what is conventionally called, by the ADA, prediabetes, and by the WHO, intermediate hyperglycemia. This is considered an intermediate stage, before the onset of diabetes, but could already be related to the risk of complications from the disease. According to different diagnostic criteria, the study identified a range from 7.5 to 17.5% of Brazilian adults who have prediabetes and intermediate hyperglycemia. A gradient of increased prevalence according to the age of the population and the presence of risk factors such as arterial hypertension, obesity, high waist circumference, and low HDL was observed. The least educated and the self-declared black had a higher prevalence. Thus, a set of risk factors common to prediabetes and intermediate hyperglycemia can be identified.

The prevalence varied by cutoff established for the glycated hemoglobin values. In any case, it can be considered that at least 7.5% of the Brazilian adult population has above normal glycaemic levels but below the cutoff point for diabetes, emphasizing the need for preventive measures regarding the disease's risk factors.

Although the prevalence of self-reported DM in different surveys¹¹⁻¹⁴ and measured by the PNS, when considering HbA1c $\geq 6.5\%$ ¹⁰, is higher among women, this study found no differences in the frequency of prediabetes/intermediate hyperglycemia by gender, in agreement with the results of the IDF⁶. On the other hand, the pattern observed increased prevalence according to the population's age, with a risk gradient given by

Table 1. Prevalences and prevalence ratio of intermediate hyperglycemia and prediabetes by sociodemographic variables and risk factors, based on ADA and WHO criteria, PNS 2014-2015 (N = 7,548).

Variables	ADA: 5.7-6.4%			WHO: 6-6.4%		
	Prev. % (95% CI)	PRcrude	PRadj [∞]	Prev. (95% CI)	PRcrude	PRadj [∞]
Total	18.5 (17.4-19.7)	-	-	7.5 (6.7-8.3)	-	-
Gender						
Male	17.2 (15.6-19)	1	1	7.0 (5.9-8.3)	1	1
Female	19.7 (18.2-21.2)	1.14*	0.99	7.9 (6.9-9)	1.12	0.9
Age group						
18-39	7.8 (6.6-9.2)	1	1	2.2 (1.6-3.1)	1	1
40-59	20.4 (18.5-22.4)	2.62*	2.15*	7.8 (6.6-9.3)	3.5*	2.53*
≥60 years	37.6 (34.7-40.5)	4.82*	3.63*	17.9(15.6-20.4)	7.98*	4.83*
Schooling						
No education to elementary	22 (20.4-23.6)	1	1	9.8 (8.6-11)	1	1
Secondary complete and over	14.5 (13-16.3)	0.66*	0.95	4.9 (4-5.9)	0.5*	0.79
Ethnicity/skin color						
White	18.8 (17.1-20.6)	1	1	7.3 (6.3-8.6)	1	1
Black	26.7 (22.3-31.6)	1.42*	1.5*	13.8 (10.3-18.4)	1.89*	2.07*
Brown	16.2 (14.8-17.7)	0.86*	0.97	6.2 (5.4-7.3)	0.85	1.04
Other	25.9 (14.7-41.5)	1.38	1.51	8.6 (2.6-25.3)	1.18	1.36
Region						
North	14.6 (13-16.3)	1	1	5.3 (4.4-6.5)	1	1
Northeast	16.4 (15-17.9)	1.13	1.02	5.8 (4.9-6.7)	1.08	0.95
Southeast	20.6 (18.5-22.9)	1.42*	1.19*	9.1 (7.7-10.8)	1.71*	1.4*
South	16.7 (14.4-19.3)	1.15	0.97	6.8 (5.4-8.6)	1.28	1.07
Midwest	20.2 (17.5-23.2)	1.39*	1.26*	7.0 (5.4-9.1)	1.31	1.18
BMI						
Underweight/normal	12.4 (11-14)	1	1	4.8 (3.8-5.9)	1	1
Overweight	19.8 (17.9-21.8)	1.59*	1.27*	7.9 (6.7-9.3)	1.65*	1.19
Obesity	29.3 (26.4-32.4)	2.35*	1.65*	12.7 (10.7-15)	2.67*	1.54*
Waist circumference						
Normal	13 (11.8-14.4)	1	1	4.5 (3.8-5.4)	1	1
High	27.7 (25.7-29.8)	2.13*	1.2*	12.4 (11-14.1)	2.73*	1.51*
Hypertension					0	
No	12.6 (11.5-13.9)	1	1	4.2 (3.5-5)	1	1
Yes	30 (27.8-32.4)	2.38*	1.32*	14.0 (12.3-15.9)	3.35*	1.55*
HDL Cholesterol						
Recommended	15.2 (13.8-16.8)	1	1	5.9 (5-6.9)	1	1
Low	22 (20.3-23.8)	1.45*	1.28*	9.2 (8.1-10.5)	1.57*	1.35*
Physical inactivity					0	
Inactive	20.2 (18.8-21.6)	1	1	8.3 (7.4-9.4)	1	1
Insufficiently active	14.6 (11.4-18.5)	0.72*	0.87	7.6 (5.3-10.7)	0.91	1.16
Active	15 (12.9-17.4)	0.75*	0.96	5.0 (3.9-6.6)	0.61*	0.85
Consumption of fruits and vegetables						
Adequate/Regular	18.4 (16.5-20.5)	1	1	7.6 (6.4-9.2)	1	1
Low	18.5 (17.2-20)	1.01	1.11	7.4 (6.5-8.4)	0.97	1.05

Source: PNS 2014-2015. Prev. = Prevalence. PR = Prevalence ratio. [∞]PRadj = PR adjusted by multivariate analysis considering all variables in the model. * Prevalence with significant differences, considering a significance level of 5%.

Table 2. Prevalence and prevalence ratio of intermediate hyperglycemia by the number of risk factors**, based on ADA and WHO criteria, PNS 2014-2015 (n = 7,297).

Variables	ADA			WHO		
	Prev. % (95% CI)	PRcrude	PRadj [∞]	Prev. (95% CI)	PRcrude	PRadj [∞]
One factor	9.1 (7.0-11.8)	1	1	2.4 (1.4-4.1)	1	1
Two factors	12.0 (10.2-14.0)	1.31	1.13	4.3 (3.3-5.7)	1.82	1.49
3-4 factors	22.3 (20.5-24.2)	2.44*	1.76*	9.1 (7.9-10.5)	3.82*	2.49*
Five factors and over	35.9 (32.1-39.9)	3.93*	2.56*	17.2 (14.3-20.6)	7.23*	4.13*

Source: PNS 2014-2015. Prev. = Prevalence. PR = Prevalence ratio. [∞]PRadj = PR adjusted by multivariate analysis considering all variables listed in the score (1, 2, 3 or 4, 5 or more) and age as a control variable. * Prevalence with significant differences, considering a significance level of 5%. ** Considering the variables: obesity, high waist circumference, high blood pressure, low HDL cholesterol, physical inactivity, and low consumption of fruits and vegetables.

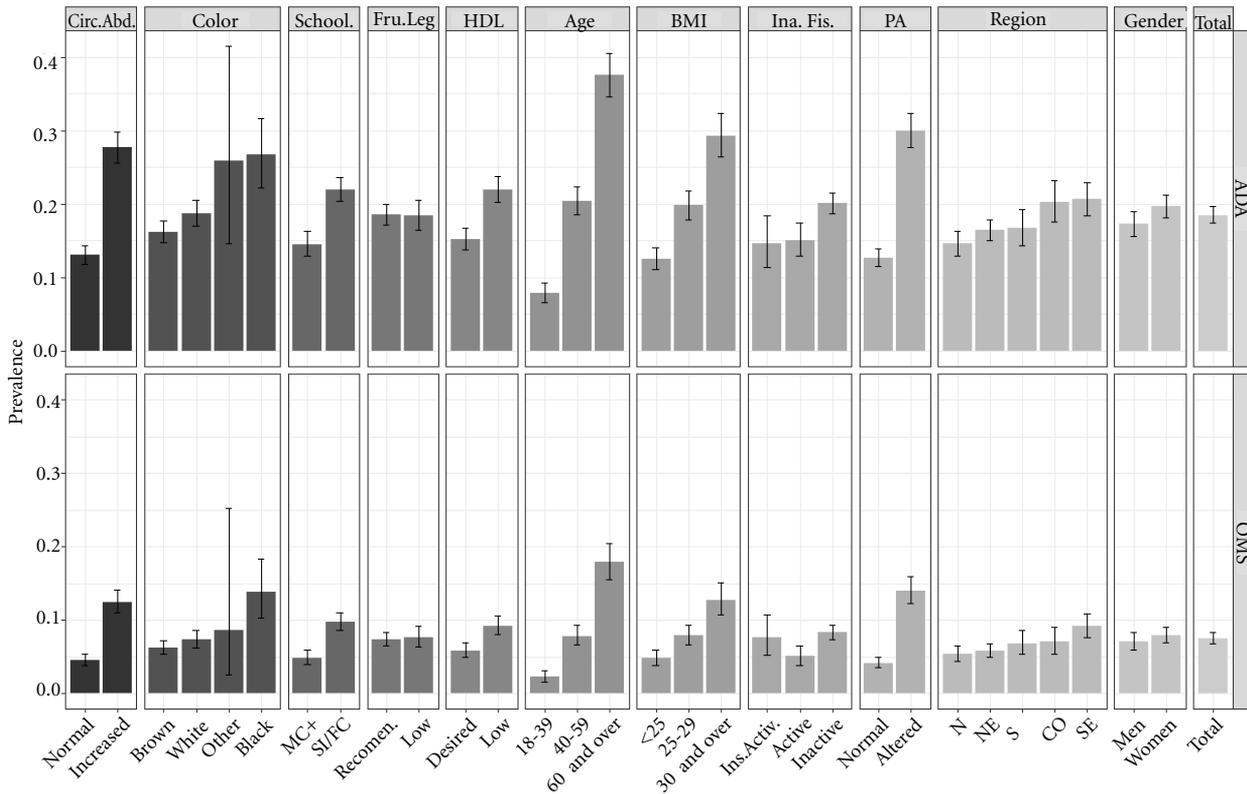


Figure 1. Prevalence of prediabetes and intermediate hyperglycemia according to sociodemographic characteristics and risk factors, based on ADA and WHO criteria, PNS 2014-2015.

Source: PNS 2014-2015.

Acronyms: Circ. Abd = High abdominal circumference: ≥ 102 cm in men / 88 cm in women. HDL (High Density Lipoproteins); Low: < 40 mg/dl for men and < 50 mg/dl for women. School. = Schooling. MC+ = complete secondary and over SI/FC = no education to complete elementary. Fru. Leg. = Consumption of fruits and vegetables; Recomen. = recommended (≥ 5 servings daily five or more times a week). BMI = Body Mass Index. Ina. Fis. = Physical inactivity. Ins. Activ. = insufficiently active (150 minutes/week). PA = Blood Pressure; PA Alter. = altered or elevated blood pressure (≥ 140 or 90 mmHg, report of medical diagnosis, or use of antihypertensive medication). N = North Region; NE = Northeast; S = South; CO = Midwest; SE = Southeast. ADA = American Diabetes Association. OMS = World Health Organization.

low schooling, obesity, and comorbidities such as arterial hypertension, besides physical inactivity, is per the occurrence of diabetes itself¹⁰⁻¹². However, in this study, the determination of the diagnostic criterion influences these relationships.

The WHO criterion may be more restrictive, meaning that more than half of the prevalence is reduced compared to ADA's criteria. Thus, it follows, in this way, that an essential portion of the population is found in the borderline blood glucose range between the two criteria (HbA1c between 5.8-5.9), and it is essential to include them in the preventive efforts to postpone the establishment of the disease. With twice the prevalence estimate with the ADA criteria, the low agreement between the tests had already been identified in a systematic review by Barry et al.¹⁵. The prevalence found when using the criteria indicated by the WHO International Committee of Experts (IEC) had 27% of prediabetes, 48% of which were identified only by the increase in HbA1c, whereas considering ADA criteria, the prevalence would be 49%, with a more significant overlap of results.

The comparison of the estimates in this study with the literature is limited due to the various criteria used and various factors interfering in the prevalence of this condition, including the population's specific characteristics⁵. In a systematic review, the prevalence of prediabetes varied widely from 27% to 66%, and, considering only abnormal HbA1c values, it ranged from 8 to 48% in different populations¹⁵.

Few Brazilian population-based studies provide estimates of prediabetes and intermediate hyperglycemia. A study carried out in the 1980s in nine Brazilian cities¹⁶ found a prevalence of glucose intolerance of 7.8% in the population aged 30-69 years. In inland Ceará, the prevalence of prediabetes was 14.2% (95% CI 11.6-16.7) in a random sample of the population ≥ 20 years of age, which was determined by fasting blood glucose between 110 and 126 mg/dL and for an OGTT result < 140 mg/dL¹⁷. Using the WHO criterion as a reference, the use of HbA1c showed an area under the ROC curve for the detection of prediabetes of 61%, indicating an ideal cutoff point of 6.0% (42 mmol/mol), with a sensitivity of 67.3% and specificity of 52%¹⁷. An evaluation of 138 patients at high risk for the development of diabetes due to the presence of metabolic conditions, such as hypertension, obesity, and dyslipidemia, was carried out in a public hospital in São Paulo¹⁸. The prevalence of prediabetic status was 68.0%, and those who had fasting blood glu-

cose and OGTT alterations were older and had more risk conditions for DM than those within normal limits. The study also showed the lack of agreement between the two tests used, and 18% had a fasting blood glucose within normal values¹⁸ among those with glucose intolerance.

It is crucial to verify possible discrepancies in prevalence by ethnicity/skin color, as HbA1c levels vary in different populations², especially in people of African descent¹⁹. In this study, the black population had a higher prevalence of prediabetes/intermediate hyperglycemia, which could be related to genetic issues, physiological characteristics of red blood cells, and cell turnover²⁰. Studies with different populations have found higher levels of HbA1c in the black population when compared to white, even after controlling for other factors such as age, access to health services, and socioeconomic status²⁰. A study with a black population in South Africa indicated that, for this population, the ideal cutoff point for the detection of diabetes by HbA1c would be 6.0% (42 mmol/mol), regardless of whether the reference test is OGTT or fasting blood glucose²¹. This result suggests that the detection of prediabetes/intermediate hyperglycemia with values adopted in this study could already point to diabetes in this population.

It is worth mentioning that the Brazilian population is quite mixed, and national results may not be comparable to those achieved outside the country, where other ethnicities predominate. Also, the ethnicity/skin color variable was self-declared, following the pattern of the Brazilian Institute of Geography and Statistics (IBGE). An evaluation with the Xavante indigenous people from the Midwest region, considered to be at high risk for diabetes, found a moderate performance (accuracy of 51.4%) of HbA1c for detecting impaired glucose tolerance in this population, in the 5.7-6.4% range²².

Previous studies have shown a higher prevalence of diabetes in the Southeast and Midwest regions¹⁰. However, when considering self-reported information, the Brazilian South and Southeast regions have generally higher prevalence, which could be related to better access to diagnosis and health care for this population²³. In this study, after adjusting the estimates for various factors such as age, schooling, ethnicity, and BMI of the population, the prevalence of prediabetes, according to the ADA criterion, and intermediate hyperglycemia, considering WHO criteria, was higher in the Southeast region of the country, suggesting that other factors, not identi-

fied in this analysis, are related to hyperglycemia in the population of that region.

The use of HbA1c for diagnosis is still controversial. A systematic review indicated a sensitivity of 49% and specificity of 79%, with an overall accuracy estimated at 71%. However, the test performance was heterogeneous according to the population and study location¹⁵. On the other hand, the argument for the inclusion of HbA1c as a method of screening and diagnosis is the possibility of verifying long-term exposure (two to three months) to high glycemic levels (baseline and postprandial), which may reflect a combination of pathophysiological conditions underlying altered fasting blood glucose and impaired glucose tolerance^{1,2}. Also, considering the logistics and costs of performing biochemical measurements at the population level, the use of HbA1c is convenient for epidemiological purposes, as it does not require fasting¹⁰, indicating individualized measures for use in the clinic, including confirmatory testing before the establishment of a specific treatment.

Screening for intermediate hyperglycemia and prediabetes is also controversial, especially since the effectiveness of screening followed by an intensive lifestyle change program was only found when the intermediate blood glucose was tested by OGTT, and such screening to achieve population outreach is underused. A recent comparison in Brazilians showed that the WHO criteria for intermediate hyperglycemia would be more predictive of diabetes²⁴.

As limitations of this study, it should be considered that the lack of consensus for the determination of prediabetes and intermediate hyperglycemia among the largest world entities prevents the determination of a single national

estimate. Furthermore, the cross-sectional nature of the survey data allows only the analysis of associations and not causality. Given the study's characteristics, the impossibility of carrying out reference tests did not allow a detailed analysis of the diagnostic criteria and glycated hemoglobin accuracy. It should also be noted that, as indicated by the literature²⁰, HbA1c values may be influenced by hemoglobinopathies, anemia, and other conditions not addressed in this study. The percentage of losses in the realization of laboratory samples, mainly due to addresses not found, reduced the actual population studied. However, post-stratification weighting was applied to maintain the sample's representativeness.

Conclusions

This study points to a range of 7.5-18.5% of Brazilian adults with intermediate prediabetes/hyperglycemia and identifies a risk score for this condition. Considering the limitations and influential factors in the measurements of glycated hemoglobin, the identification of a set of risk factors common to the occurrence of diabetes and its complications, such as age, ethnicity, and biological markers such as for overweight and increased waist circumference, hypertension arterial, and low HDL cholesterol, can assist in recommending specific tests and analyses in each population stratum to better define priority groups for timely interventions. Thus, the study fulfills its epidemiological purpose of updating national estimates of an essential portion of the population at high risk for the development of diabetes, subsidizing health planning and surveillance actions, also reaching an objective of the PNS itself.

Collaborations

BPM Iser participated in the conception and design of the study, organization, analysis, and interpretation of the data, and was responsible for the first version of the manuscript. PC Pinheiro was responsible for data extraction and analysis, contributed to their interpretation, and drafting of the manuscript. DC Malta, BB Duncan and MI Schmidt contributed to the study's conception and design, analysis, and interpretation of the data and participated in scientific writing. All authors approved the final version to be published and are responsible for its content.

References

1. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020. *Diabetes Care* 2020; 43(Supl. 1):S14-31.
2. Sequeira IR, Poppitt SD. *HbA1c as a marker of prediabetes: A reliable screening tool or not. Insights in Nutrition and Metabolism* [Internet]. 2017 [acessado 2020 Maio 12]; 1(1). Disponível em: <https://www.alliedacademies.org/abstract/hba1c-as-a-marker-of-prediabetes-a-reliable-screening-tool-or-not-7025.html>
3. Zhang X, Gregg EW, Williamson DF, Barker LE, Thomas W, Bullard KM, Imperatore G, Williams DE, Albright AL. A1C level and future risk of diabetes: a systematic review. *Diabetes Care* 2010; 33(7):1665-1673.
4. World Health Organization (WHO). *Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia* [Internet]. WHO; 2006 [acessado 2020 Maio 13]. 46 p. Disponível em: https://www.who.int/diabetes/publications/diagnosis_diabetes2006/en/
5. Hostalek U. Global epidemiology of prediabetes - present and future perspectives. *Clin Diabetes Endocrinol* [Internet] 2019 [acessado 2020 Maio 13]; 5. Disponível em: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6507173/>
6. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala AA, Ogurtsova K, Shaw JE, Bright D, Williams R, On behalf of the IDF Diabetes Atlas Committee. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Research and Clinical Practice* [Internet]. 2019 [acessado 2020 Maio 12]; 157. Disponível em: [https://www.diabetesresearchclinicalpractice.com/article/S0168-8227\(19\)31230-6/abstract](https://www.diabetesresearchclinicalpractice.com/article/S0168-8227(19)31230-6/abstract)
7. Sociedade Brasileira de Diabetes. *Diretrizes da Sociedade Brasileira de Diabetes 2019-2020* [Internet]. SBD; 2019 [acessado 2020 Maio 12] p. 490. Disponível em: <https://www.diabetes.org.br/profissionais/images/DIRETRIZES-COMPLETA-2019-2020.pdf>
8. World Health Organization (WHO). Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus. *Diabetes Res Clin Pract* 2011; 93(3):299-309.
9. Szwarcwald CL, Malta DC, Pereira CA, Vieira MLFP, Conde WL, Souza Júnior PR, Damacena GN, Azevedo LO, Azevedo E Silva G, Theme Filha MM, Lopes CS, Romero DE, Almeida WS, Monteiro CA. National Health Survey in Brazil: design and methodology of application. *Cien Saude Colet* 2014; 19(2):333-342.
10. Malta DC, Duncan BB, Schmidt MI, Machado IE, Silva AG, Bernal RTI, Pereira CA, Damacena GN, Stopa SR, Rosenfeld LG, Szwarcwald CL. Prevalência de diabetes mellitus determinada pela hemoglobina glicada na população adulta brasileira, Pesquisa Nacional de Saúde. *Rev Bras Epidemiol* [Internet]. 2019 [acessado 2020 Maio 29]; 22. Disponível em: http://www.scielo.br/scielo.php?script=sci_abstract&pid=S1415-790X2019000300408&lng=en&nrm=iso&tlng=pt
11. Iser BPM, Stopa SR, Chueiri PS, Szwarcwald CL, Malta DC, Monteiro HOC, Duncan, Bartholow BD, Schmidt MI. Prevalência de diabetes autorreferido no Brasil: resultados da Pesquisa Nacional de Saúde 2013. *Epidemiologia e Serviços de Saúde* 2015; 24(2):305-314.

12. Iser BPM, Vigo A, Duncan BB, Schmidt MI. Trends in the prevalence of self-reported diabetes in Brazilian capital cities and the Federal District, 2006-2014. *Diabetology and Metabolic Syndrome* [Internet]. 2016 [acessado 2020 Maio 29]; 8(1). Disponível em: <http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L612834024>
13. Stopa SR, Cesar CLG, Segri NJ, Alves MCGP, Barros MBA, Goldbaum M. [Prevalence of arterial hypertension, diabetes mellitus, and adherence to behavioral measures in the city of São Paulo, Brazil, 2003-2015]. *Cad Saude Publica* 2018; 34(10):e00198717.
14. Miraglia JL, Mafra ACCN, Monteiro CN, Borges LM. The variation of the burden of hypertension and diabetes in two large districts of the city of São Paulo, Brazil, based on primary health care routinely-collected data. *PLoS One* 2019; 14(3):e0213998.
15. Barry E, Roberts S, Oke J, Vijayaraghavan S, Normansell R, Greenhalgh T. Efficacy and effectiveness of screen and treat policies in prevention of type 2 diabetes: systematic review and meta-analysis of screening tests and interventions. *BMJ* 2017; 356:i6538.
16. Malerbi DA, Franco LJ. Multicenter study of the prevalence of diabetes mellitus and impaired glucose tolerance in the urban Brazilian population aged 30-69 yr. The Brazilian Cooperative Group on the Study of Diabetes Prevalence. *Diabetes Care* 1992; 15(11):1509-1516.
17. Moreira NCV, Montenegro RM, Meyer HE, Bhowmik B, Mdala I, Siddiquee T, Fernandes VO, Hussain A. Glycated Hemoglobin in the Diagnosis of Diabetes Mellitus in a Semi-Urban Brazilian Population. *Int J Environ Res Public Health* 2019; 16(19):3598.
18. Matos LN, Giorelli GV, Saado A, Dias CB. Prevalence of prediabetes in patients with metabolic risk. *Sao Paulo Med J* 2011; 129(5):300-308.
19. Ziemer DC, Kolm P, Weintraub WS, Vaccarino V, Rhee MK, Twombly JG, Narayan KMV, Koch DD, Phillips LS. Glucose-independent, black-white differences in hemoglobin A1c levels: a cross-sectional analysis of 2 studies. *Ann Intern Med* 2010; 152(12):770-777.
20. Herman WH, Cohen RM. Racial and ethnic differences in the relationship between HbA1c and blood glucose: implications for the diagnosis of diabetes. *J Clin Endocrinol Metab* 2012; 97(4):1067-1072.
21. Hird TR, Pirie FJ, Esterhuizen TM, O'Leary B, McCarthy MI, Young EH, Sandhu MS, Motala AA. Burden of Diabetes and First Evidence for the Utility of HbA1c for Diagnosis and Detection of Diabetes in Urban Black South Africans: The Durban Diabetes Study. *PLoS One* 2016; 11(8):e0161966.
22. Franco LJ, Dal Fabbro AL, Martinez EZ, Sartorelli DS, Silva AS, Soares LP, Franco LF, Kuhn PC, Vieira-Filho JPB, Moisés RS. Performance of glycated haemoglobin (HbA1c) as a screening test for diabetes and impaired glucose tolerance (IGT) in a high risk population--the Brazilian Xavante Indians. *Diabetes Res Clin Pract* 2014; 106(2):337-342.
23. Malta DC, Stopa SR, Iser BPM, Chueiri PS, Duncan BB, Schmidt MI, Duncan BB. Cuidados em saúde entre portadores de diabetes mellitus autorreferido no Brasil, Pesquisa Nacional de Saúde, 2013. *Rev Bras Epidemiol* 2015; 18(Supl. 2):17-32.
24. Schmidt MI, Bracco PA, Yudkin JS, Bensenor IM, Griep RH, Barreto SM, Castilhos CD, Duncan BB. Intermediate hyperglycaemia to predict progression to type 2 diabetes (ELSA-Brasil): an occupational cohort study in Brazil. *Lancet Diabetes Endocrinol* 2019; 7(4):267-277.

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