Pre-diabetes: The Need for Screening and Diagnosis to Prevent Rising Prevalence in the Future

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Abstract: An approximated 240 million people are living with undetected diabetes across the globe. Astonishingly, almost one-in-two adults with diabetes are not aware of the condition. Such population is at an elevated risk of diabetic complications. Additionally, several others are living with the risk factors like age, obesity, family history of diabetes, lack of physical activity, and hypertension. Screening at the population level may include both blood glucose testing and through questionnaire based tool viz. Indian Diabetes Risk Score (IDRS). IDRS is a useful tool to segregate high-risk populations who may be further tested for a confirmed diagnosis of diabetes. 75-gram oral glucose tolerance test is being advocated as a more accurate method to diagnose pre-diabetes. Extensive screening of the populace for the diagnosis of diabetes and pre-diabetes would enable appropriate management, thereby reducing their conversion to confirmed cases and, supporting reversal to normoglycemic status, and, halting the ever-increasing numbers of diabetes.

Keywords: Diabetes, Diabetes risk assessment, Diabetes screening, Glucose monitoring, HbA1c, IDRS, Pre-diabetes, Undiagnosed diabetes.

I. Introduction

One of the leading causes of mortality due to non-communicable diseases, the prevalence of diabetes and pre-diabetes has attained epidemic levels. A significant proportion of the population remains undetected, [1] which silently progresses towards diabetes-related complications. To put a halt to the increasing numbers, screening and timely diagnosis at the populace level are the need of the hour. Screening can be done through a non-invasive questionnaire based tool- Indian Diabetes Risk Score (IDRS).^[2] Alternatively, blood tests can be performed to quantify blood glucose levels. IDRS can be implemented at the masses level to sieve out the high-risk individuals who can then be further tested for clinical diagnosis of the pre-diabetes or diabetes. Well-timed diagnosis of pre-diabetes brings forth the great potential of reversing the condition to healthiness, and also reducing the upcoming micro and macro-vascular complications.

II. Pre-diabetes

The term "pre-diabetes" refers to a clinical condition wherein the measured blood glucose levels are higher than the normal range, but below the diabetes diagnostic threshold for a confirmed diagnosis of diabetes.^[3] The alternative terminologies for 'pre-diabetes' are 'non-diabetic hyperglycemia,^[4] and 'intermediate hyperglycemia.^[5] On the other hand, undiagnosed diabetes is defined as a condition wherein the blood sugar levels of a person fall above the clinical diagnostic threshold, but the diagnosis has not been confirmed by a medical practitioner.^[6]Derangement in blood glucose level in pre-diabetes is measured by impaired

glucose tolerance IGT or impaired fasting glucose IFG. Patients can have either or both of the given conditions to be considered pre-diabetic

III. Global Burden

Taking the world by the storm, the prevalence of diabetes and pre-diabetes is increasing at a threatening pace. Revealed by International Diabetes Federation in the Tenth edition of Diabetes Atlas, diabetes is one of the silently growing global health emergencies of the 21st century. In 2021, 541 million adults, or 10.6% of adults worldwide, were estimated to have impaired glucose tolerance (IGT). By 2045, these figures are projected to increase to 730 million adults, or 11.4% of all adults. In 2021, there were an estimated 319 million adults, or 6.2% of the global adult population, with impaired fasting glucose (IFG). An estimated 441 million adults or 6.9% of the global adult population are projected to have IFG in 2045. Estimated for undiagnosed diabetes, reported in 2021, almost one in two (44.7%; 239.7 million) adults living with diabetes (20–79 years old) are unaware of their glycemic status. [6]

The figures for India are equally alarming. Globally ranked at second position in 2021, the prevalence of Diabetes in India is 8.3%. The present 74.2 million diabetic adult Indian Population is expected to increase to 124.9 million by the year 2045, anticipated to retain the same rank in the coming years too. [6] In 2021, the age-adjusted comparative prevalence of IGT was 5.4% (3.2-9.6%) which counted 40 million adults. On the other hand, the age-adjusted comparative prevalence of IFG was 7.8% (4.6%- 18.1%) which accounted for 75 million adults. A huge quantum i.e. 53.1 % proportion of the Indian adult population (39 million) is expected to be holding undiagnosed diabetes. [6]

IV. Screening and Diagnostic criteria

An estimated 39 million Indians with undiagnosed diabetes, 75 million Indians with IFG and, 40 million Indians with IGT, the numbers are huge and overwhelming. In addition to this are the individuals falling into several risk groups; obese subjects, having a family history of diabetes, having hypertension and, following no physical activity.^[7] Screening all the numbers through blood tests would be huge. The most economical way to screen these individuals is by implementing the scientifically validated, questionnaire-based tool IDRS,^[2] presented in Table 4.1

Table 4.1: Indian Diabetes Risk Score

Indian Diabetes Risk Score					
Risk factors	Parameters	Score			
Age	<35 years	0			
	35-49 Years	20			
	≥50 years	30			
Abdominal	Waist circumference <80 cm (female), <90cm (male)	0			
obesity	Waist circumference 80-89 cm(female), 90-99cm (male)	10			
	Waist circumference ≥ 90 cm (female), ≥100cm (male)	20			
Physical activity	Regular vigorous exercise or strenuous (manual) activities at	0			
	home/work				
	Regular moderate exercise or moderate physical activity at				
	home/work				
	Regular mild exercise or mild physical activity at home/work	20			
	No exercise and/or sedentary activities at home/work	30			
Family history	Both parents non-diabetic	0			
	Either parent diabetic	10			
	Both parents diabetic	20			

The tool was created by Dr. V Mohan in the year 2005,^[2] at Madras Diabetes Research Foundation, Chennai. The total scores of the subject are analyzed for categorization into risk categories; a score of less than 30 corresponds to low risk, a Sum of the scores in the range of 30-50 corresponds to moderate risk, and a sum of the scores greater than or equal to 60 indicates high risk for diabetes. Widely utilized in community research, presenting great specificity and

sensitivity, this tool can accomplish screening of the masses cost-effectively in minimum time. It can help segregate the high-risk individuals who can further be directed to the practicing clinicians for confirming the diagnosis of the disease.

An alternate way to confirm the diagnosis is through blood tests. Clinical screening can be performed by testing fasting plasma glucose, an oral glucose tolerance test (OGTT) using 75 gram glucose or random plasma glucose. Glycosylated (glycated) hemoglobin (HbA1c) is also recommended for clinical screening and confirmation. The world health organization^[8], and the American diabetes association^[9], have laid down respective diagnostic criteria for the diagnosis of diabetes and pre-diabetes presented in Table 4.2

Table 4.2: Diagnostic criteria for Diabetes and Pre-diabetes

Parameter	Normoglycemia		Pre-diabetes (mg/dl)		Diabetes (mg/dl)
	(mg/dl)				
	WHO	ADA	WHO	ADA	
FBG*	<110	<100	110-125	100-125	More than or equal to
			(IFG)	(IFG)	126
2-h PG	<140		140-199 (IGT)		More than or equal to
					200
HbA1c	<5.7%			5.7-6.4%	<u>≥</u> 6.5%
Random Plasma					\geq 200 (with symptoms
Glucose †					of disease)

^{*} Fasting is defined as no calorie intake for at least eight hours.

WHO recommends the testing of HbA1c \geq 6.5% for the diagnosis of diabetes but finds it inadequate for diagnosis of pre-diabetes.^[10] There is cumulative authentication favoring the use of 75 gram OGTT as a more accurate method of diagnosing pre-diabetes.^[11] Presently, both WHO and IDF advocate the use of 75 gram oral glucose tolerance test (OGTT) along with quantification of fasting blood glucose levels to diagnose IFG AND IGT.^[6]

[†] Individuals with random plasma glucose ranging between 140-199mg/dl are advised to undergo OGTT. WHO - World Health Organization; ADA-American Diabetes Association; IFG - Impaired Fasting Glucose; IGT - Impaired Glucose tolerance; FPG - Fasting Plasma Glucose; 2-h PG-2 hour post load Glucose test (oral glucose tolerance test); HbA1c - Glycosylated Hemoglobin

V. Why should we worry about pre-diabetes?

Diabetes mellitus is a systemic disorder, primarily defined by the derangement in the blood glucose levels; which has adverse effects on the micro-vascular system (retinopathy, nephropathy, and neuropathy)^[7,12-14] as well as the macro-vascular system (ischemic heart disease, stroke, and peripheral vascular diseases),^[7,13,15-16] thereby reducing the life expectancy and consequential morbidity. Significantly put, the progressive complications of the deranged blood sugar levels are not constricted to diabetes only. Complications of lesser degree have been documented in the normal populations and pre-diabetes too.^[17]

Pre-diabetes is a dominant indicator of the development of type 2 diabetes. ^[6] According to an expert panel of the American diabetes association, up to 70% of individuals with pre-diabetes will eventually develop diabetes. ^[18] Given, that no preventive measures in place, pre-diabetes progresses to conspicuous diabetes at the rate of approximately 5% per year. ^[7] The cumulative incidence of type 2 diabetes at 5 years post-diagnosis of IFG/IGT is estimated to be 26% and 50%, respectively. ^[6]

Both diabetes and pre-diabetes are correlated with vascular complications.^[7] The presence of pre-diabetes predicts a high risk for the development of atherosclerotic vascular disease and cardiovascular disease.^[7,19] Several Studies have been documented indicating an elevated risk of cardiovascular disease prior to the diagnosis of type 2 diabetes.^[7,19-20] In an investigation of data from NHANES 2011-2014, subjects with pre-diabetes (diagnosed based on ADA-FPG test or HbA1c testing) indicated an elevated prevalence of dyslipidemia (51.2%), hypertension (36.6%), albuminuria (7.7%) or decreased estimated glomerular filtration rate (4.6%).^[20] To substantiate, a meta-analysis of 53 prospective studies which included 1.6 million subjects suggested a strong association between pre-diabetes and an elevated risk of cardiovascular

disease.^[19] Therefore, any overlooked case of pre-diabetes is also a case of overlooked cardiovascular disease.

Convincingly, the diagnosis of pre-diabetes is advantageous. It signals the risk for the development of type 2 diabetes in the future, suggests an existing or expected elevated risk of cardiovascular diseases, [7,19-20] and its diagnosis paves the way for the interventions to reverse the state or prevent further progression to full-blown diabetes.

VI. Conclusion

Global estimates of pre-diabetes and undiagnosed diabetes are sizeable and projected to elevate by 2045, suggesting crucial challenges for the future risk of diabetes worldwide. A concurrent increase in the prevalence in the Indian population makes screening imperative at the national level. Although the clinical confirmation of the disease can be done only through blood tests, the risk assessment can be performed through the non-invasive Indian Diabetes Risk Score Tool. This would enable timely diagnosis and prevention of the disease thus reducing the burden of diabetes on the nation. Regular testing is significant to diagnose, prevent or delaying advancement of diabetes in the future.

"It is imperative to see pre-diabetes as a disease state which needs attention and resolution."

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