



How to diagnose prediabetes

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***Brit Med. J* series on overdiagnosis**

Intermediate hyperglycemia was named first „impaired glucose tolerance”, since 1997 the term „impaired fasting glucose” was created , in 2010 the intermediate category based on HbA1c was designated.

***Brit Med. J* series on overdiagnosis**

The value of a diagnosis of prediabetes would be that it „can provide benefit precisely identifying those who will develop diabetes, allowing for effective interventions targetting both the disease and its complications”

Yudkin and Montori

***Brit Med. J* series on overdiagnosis**

Whether a diagnosis of prediabetes guarantees a future diagnosis of diabetes ?

„No- less than 50% of all such people develop diabetes within 10 years”

Yudkin and Montori

Aldous Huxley

„Medical science has made such tremendous progress that there is hardly a healthy human left“

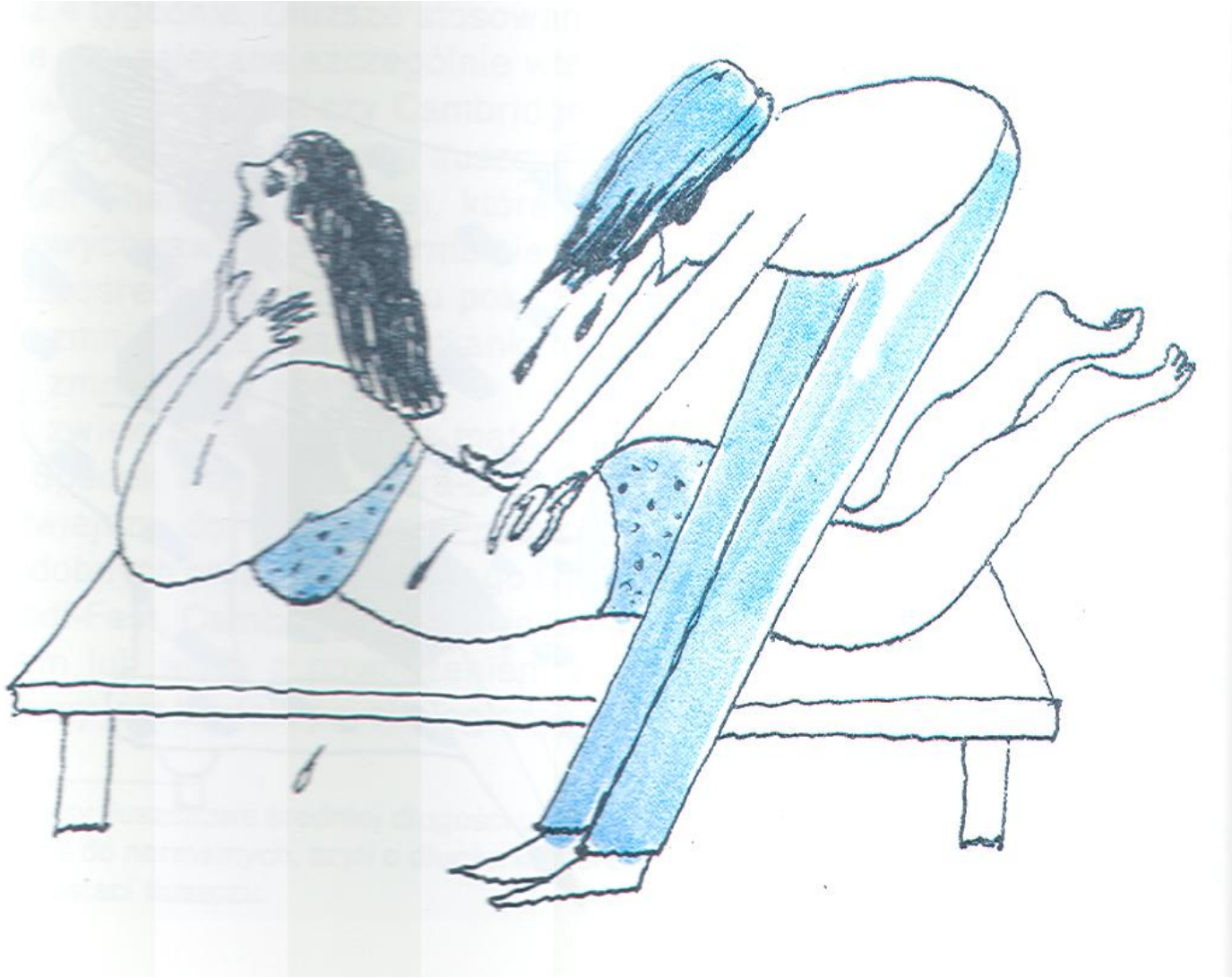
**Prediabetes is the condition with impaired fasting glucose (IFG), glucose concentrations higher than normal but below the established threshold for diabetes,
or impaired glucose tolerance (IGT) recognized based on the results of a 2-hour oral glucose tolerance test (OGTT).**

People with prediabetes are at high-risk for developing diabetes and associated complications.

It is estimated that each year 5-10% of individuals with prediabetes will develop T2 diabetes.

IFG and/or IGT are associated with abdominal or visceral obesity, high serum Tg and/or low HDL-C, hypertension.

In subjects with IGT lifestyle changes such as increase of physical activity, losing weight (5-10%) and pharmacological therapy may prevent or delay the development of diabetes.



Diagnosis of prediabetes

World Health Organization (WHO) criteria for impaired fasting glucose differ from the American Diabetes Association (ADA 2010) criteria, because the normal range of glucose is defined differently.

Diagnosis of prediabetes

WHO criteria

FPG

110-125 mg/dL
(6.1- 6.9 mmol/L)

2-hr OGTT-glucose
140-198 mg/dL
(7.8-11.0mmol/L)

HbA1c

5.7-6.4%
(39-47 mmol/mol)

ADA criteria

FPG

100-125 mg/dL
(5.6- 6.9 mmol/L)

2-hr OGTT-glucose
140 -198 mg/dL
(7.8-11.0 mmol/L)

HbA1c

5.7-6.4%
(39-47 mmol/mol)

Diagnosis of prediabetes

According to ADA criteria (2010) the recommended order for prediabetes testing is as follows: **HbA1c, FPG and/or OGTT.**

Controversy on whether HbA1c -should be used as the only test and 2-hr OGTT brings an added value.

Diagnosis of prediabetes

HbA1c-defined prediabetes ranges - a subject of debate, some favouring

6.0-6.4% (42-47 mmol/mol) instead of 5.7-6.4%.

FPG is recommended to be measured in venous plasma.



Diagnosis of prediabetes

- **Analytical methods for glucose and HbA1c may affect the interpretation of results.**

It is important - both FPG and glucose tolerance test reflect distinct processes.

Normal FPG reflects - adequate insulin secretion and control of hepatic glucose output whereas normal GT indicates adequate secretion of insulin and insulin sensitivity in the target tissues.

This explains why an individual with impaired fasting glucose may have IGT or even diabetes and individual with normal FPG may have IGT.

Screening for prediabetes

Screening for prediabetes should add FPG for those with HbA1c of 6.0-6.5%.

Controversies in specific populations (Asians) whether using only HbA1c and FPG without OGTT for detecting prediabetes, leads to false negative results.

It seems clear that individuals with HbA1c of 6.0-6.5% are in the high-risk group and, the estimated risk of mortality and CVD showed the strongest association with the results of OGTT than FPG or HbA1c.

HbA1c advantages

**OGTT, comparing to HbA1c,
is more difficult to perform and time-consuming.**

HbA1c concentration may be affected by red blood cell survival time, ethnicity, age and renal function but has several advantages.

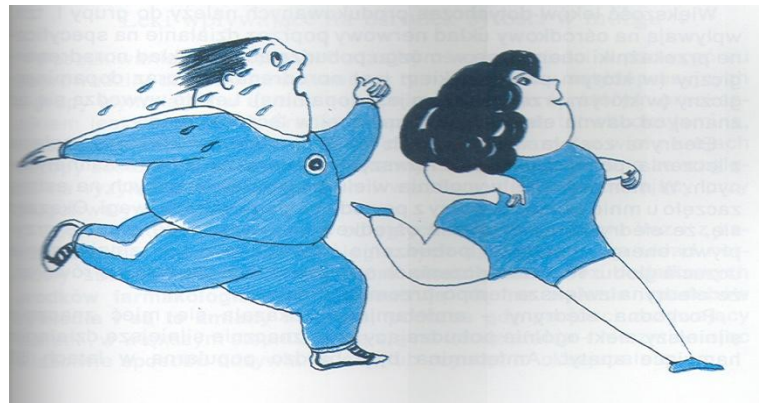
Comparing to fasting glucose, HbA1c has a small intraindividual variability, good stability after blood collection and no need for fasting.

Prediabetes

Recent data from the Centre for Disease Control showed that

~30% of adults in US have prediabetes defined based on FPG 100-125 mg/dL or HbA1c 5.7-6.4%.

Without weight loss and increased physical activity 15-30% of Americans with prediabetes will progress to T2D within 5 years.



Prevalence of prediabetes in adults

Korean population - prevalence of diabetes and prediabetes evaluated according to FPG alone or the combination : FPG and HbA1c.

HbA1c measured with HPLC.

The prevalence of prediabetes was

FPG	FPG + HbA1c
19,3%	38,3%

Adding HbA1c as complementary test to FPG allow to avoid underestimation of the diabetes and prediabetes prevalence.

Screening for prediabetes

South Asian individuals aged 18-60 years were screened performing OGTT and HbA1c measurements.

Out of 353 cases meeting HbA1c prediabetes criteria only 62 met OGTT criteria (18%).

The optimal threshold for HbA1c for predicting prediabetes in this study was 5.8-6.3% (40-45 mmol/mol Hb).

Individuals with prediabetes identified with HbA1c criteria had a high body mass index, hypertension and low insulin sensitivity.

Conclusion: each test identifies partially different group of subjects and HbA1c only should not be used for detection of prediabetes.

Screening for prediabetes

In a middle-aged and elderly Han Chinese population from northwest China

HbA1c with the threshold of 6.1% showed to be an effective and convenient test for identifying prediabetes.



Screening for prediabetes

Recent report from England on the prevalence of prediabetes in individuals 16 -75 years in the period from 2003 to 2011.

The prevalence, defined as HbA1c 5.7- 6.4%
11.6% ↗ 35.3%.

Within these 8 yrs 50.6% of overweight individuals >40 yrs developed prediabetes.

These findings were not affected by the methodological issues as the HbA1c measuring devices were calibrated.

Screening for prediabetes

Study from England on community based population compared diagnostic accuracy of HbA1c in screening for IFG with standard criteria 5.6-6.9 mmol/l (100-125 mg/dL).

Defining prediabetes at a lower HbA1c threshold of 39 mmol/mol (5.7%) instead of 47 mmol/mol (6.4%) increases its sensitivity in diagnosing IFG that allows to detect 40% more prediabetics.

Prediabetes

Regarding recent ADA and joint Europ Society of Cardiology and Europ Assoc for the Study of Diabetes guidelines, it is important to point out that

HbA1c <5.7% do not reliably exclude the presence of prediabetes.

The above presented data support the idea for greater use of OGTT in combination with FPG for diagnosis of dysglycemia.

Prediabetes in children and adolescents

Prevalence have increased among overweight and obese youth that has implications for long-term health.

The reviewed literature on current screening programs, diagnosis, and treatment of prediabetes at 25 childhood obesity hospital treatment centers in UK revealed :

-current prediabetes diagnostic criteria are derived from adult-based studies and not modified in respect to the lower age group.



Prediabetes in children and adolescents

There is some evidence on beneficial effects of preventing programs in children which result in a high proportion of obese with prediabetes returning to normoglycemia without pharmacotherapy.



Prediabetes in children and adolescents

In Chinese adolescents (11-16 yrs) without known diabetes the performance of HbA1c in detecting prediabetes was evaluated as well its association with cardiometabolic risk.

Prediabetes diagnosed according to ADA with HbA1c, FPG and OGTT in all with HbA1c within 5.7-6.4%.

ROC for HbA1c to identify prediabetes diagnosed by OGTT had an AUC=0.53.

These findings indicate a weak agreement between HbA1c and FPG or OGTT in detecting prediabetes in adolescents.

Future perspectives

Recently discovered adipocytokine

SFRP4 (secreted frizzled-related protein 4)

has been described as a potential biomarker of early pancreatic β -cells dysfunction.

Expression of SFRP4 mRNA and secretion of this protein from VAT is increased in obesity and correlates with insulin resistance.

A significant inverse correlation of SFRP4 expression in human pancreatic islets with insulin secretion and positive relationship with HbA1c was observed.

Future perspectives

SFRP4 is elevated in the serum **several years before clinical diagnosis of diabetes**, its presence increases the risk of diabetes up to 5x.

SFRP4 might be used as an early risk predictor of prediabetes/ diabetes, especially in apparently healthy individuals.

SFRP4 should meet general requirements for biomarkers prior to its application in routine clinical practice.



• Thank you for attention