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ORIGINAL RESEARCH

Evaluation of glycated hemoglobin (HbA1c) for the diagnosis of type 2 diabetes and prediabetes in the Palestinian Arab population - Evidence review

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1. ABSTRACT

The original study compared glycated hemoglobin, or HbA1c, with fasting plasma glycemia in 1,370 Palestinian Arab adults without known diabetes. The goal was to establish how well HbA1c identified diabetes and prediabetes compared to fasting glycemia. For diabetes, an HbA1c value of 6.3% showed the best balance between sensitivity and specificity; the 6.5% threshold, on the other hand, increased specificity, i.e., the ability to avoid false-positive classifications. The concordance between the two tests was found to be moderate for diabetes and low for prediabetes.In the section dedicated to glycated hemoglobin, “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi uses this research to explain that HbA1c and fasting glycemia are not interchangeable tests: they describe different aspects of glucose exposure and only partially identify the same individuals. Meta-analysis, population studies, and international analyses confirm this discrepancy and the high specificity of the 6.5% threshold. However, it remains necessary to interpret each result within the clinical context and, when tests do not agree, to resort to appropriate confirmation.

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MISSION

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Through articles, reviews, in-depth analyses and expert contributions, the Journal champions evidence-based medicine and science, fostering a correct interpretation of scientific data and countering misinformation. Every piece of content is developed with the aim of translating the complexity of research into understandable, useful and applicable information, while keeping intact the principles of accuracy, transparency and scientific independence.

Free from political, industrial and commercial influence, the journal stands as an authoritative and independent editorial space, dedicated to promoting scientific culture, professional development and the growth of health awareness among the public.

2. ANALYZED STUDY

The research question was whether HbA1c could be used to identify type 2 diabetes and prediabetes in Palestinian Arab adults, by comparing it with fasting plasma glucose. HbA1c indicates the proportion of red blood cell hemoglobin to which glucose has spontaneously bound; since red blood cells circulate for several months, this value roughly reflects average glucose exposure over the preceding period. Fasting blood glucose, on the other hand, provides a snapshot of glucose at a single moment after fasting.The publication is relevant to the section "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi because it directly documents that the two tests only partially classify the same individuals. The study does not prove that one test is universally superior to the other, nor does it establish which method should be applied to all populations. Instead, it shows, in a specific Palestinian sample, that the choice of the HbA1c threshold alters sensitivity, specificity, and the number of people classified with diabetes or prediabetes.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The authors conducted a cross-sectional study (an assessment carried out over a specific period, without following participants over time). They recruited 1,370 adults over the age of 30—468 men and 902 women—through voluntary access to clinics in refugee camps in the central and southern West Bank. Subjects with previously diagnosed diabetes or hemoglobinopathies, which are hereditary hemoglobin alterations that can make HbA1c measurements less reliable, were excluded.After a 10-12 hour Fasting period, participants' fasting plasma glycemia, HbA1c, lipid profile, blood pressure, and body mass index (BMI)—the ratio of weight to height used to classify overweight and obesity—were measured. HbA1c was measured using high-performance liquid chromatography, a laboratory technique that separates and quantifies different blood components. For comparison, the authors defined diabetes as a fasting glycemia of 126 mg/dL or higher, and prediabetes as values between 100 and 125 mg/dL.The performance of HbA1c was evaluated using ROC (receiver operating characteristic) curves, which compare sensitivity and specificity at different thresholds. Sensitivity indicates how many positive cases according to the reference test are identified; specificity indicates how many subjects without the condition are correctly classified as negative. The area under the curve (AUC) and the kappa coefficient—a measure of agreement between two classifications beyond what would be expected by chance—were also calculated. No follow-up is reported, consistent with the cross-sectional study design.

4. RESULTS

For diabetes, HbA1c showed a fair discriminatory ability compared to fasting glycemia: the AUC was 0.819. In practical terms, the test separated people classified with diabetes by fasting glycemia from those not classified as such quite well, but not perfectly. For prediabetes, the AUC was lower, at 0.639, indicating limited performance.The HbA1c threshold of 6.3% or higher provided the best balance observed in the study: 65.6% sensitivity, 94.5% specificity, and an average discriminatory ability of 80.0%. With the international threshold of 6.5%, sensitivity decreased to 57.4%, while specificity increased to 97.1%. This means that the higher threshold reduced false positives but identified a smaller proportion of people who were diabetic according to fasting glycemia.Out of 1,370 participants, 61 people, or 4.5%, were classified with diabetes by fasting glycemia; 73, or 5.3%, by an HbA1c of 6.5% or higher. Only 35 subjects met both criteria. The agreement between the two methods for diabetes was moderate, with a kappa of 0.498. For prediabetes, the difference was even more evident: HbA1c between 5.7% and 6.4% classified 628 people, or 45.8%, while fasting glycemia classified 337, or 24.6%; 193 people met both criteria. The kappa for prediabetes was 0.142, indicating limited concordance.The study also observed that HbA1c and fasting glycemia increased significantly as BMI increased. However, because the analysis is cross-sectional, this association does not prove that the increase in BMI directly caused the higher values measured in the individual participant.

5. INTERPRETATION

The main result is simple: fasting glycemia and HbA1c do not measure exactly the same biological phenomenon. The former primarily describes the level of glucose present in the blood after fasting; the latter summarizes the exposure of red blood cells to glucose over the preceding weeks. It is therefore plausible for a person to have a non-diagnostic fasting glycemia but an elevated HbA1c, or vice versa.This is the part of the book's narrative that is truly supported by the publication: HbA1c and fasting glycemia identify partially overlapping populations and should not be treated as perfectly equivalent measures. This finding is particularly clear for prediabetes, for which concordance was low.The 6.5% threshold favored specificity. In other words, a positive result at this threshold was rarely observed in those who were not diabetic according to fasting glycemia, but a portion of people who were positive for fasting glycemia were not identified by HbA1c. This does not prove that 6.3% is a valid diagnostic threshold in all populations, because the sample was a convenience sample, came from specific areas of the West Bank, and used fasting glycemia—not the oral glucose tolerance test—as a comparison.

6. INDEPENDENT CONFIRMING EVIDENCE

A systematic review and meta-analysis of 37 studies evaluated the accuracy of various tests for diagnosing diabetes and prediabetes in adults without a prior diagnosis, using the oral glucose tolerance test as a comparison. At the HbA1c threshold of 6.5%, the pooled sensitivity was 50.0% and the specificity was 97.3%. The result confirms the passage in the book stating that this threshold prioritizes the certainty of a positive test over the identification of all cases. The optimal threshold estimated by the authors, 6.03%, increased sensitivity to 73.9% but reduced specificity to 87.2%. However, heterogeneity between studies and populations limits the application of a single threshold value to every context [1].A population-based study conducted in Ho Chi Minh City, Vietnam, analyzed 3,523 adults aged at least 30. HbA1c classified 9.7% as having diabetes and 34.6% as having prediabetes, while fasting glycemia classified 6.3% and 12.1%, respectively. The overall agreement, kappa 0.55, was moderate, and the discordance was concentrated primarily in prediabetes. This independent validation directly confirms the Palestinian observation: the two tools do not always identify the same individuals [2].An international analysis by the NCD Risk Factor Collaboration pooled data from 364,825 adults without known diabetes, from 117 studies in 45 countries. Among people with diabetes identified at screening by at least one of the two tests, only 29-39% had both values above the threshold across different world regions; the remaining 61-71% showed an isolated elevation of fasting glycemia or HbA1c. This reinforces the idea that the discordance is not peculiar to the Palestinian sample and that its direction can vary between regions and populations [3].Taken together, these findings support a consistent chain: biologically different measures of glucose produce partially different classifications; the 6.5% HbA1c threshold is highly specific but less sensitive; therefore, combining or confirming with other tests can be informative when the clinical picture and the individual result do not coincide.

7. CONFLICTING EVIDENCE

A systematic review with network meta-analysis, based on 73 studies and using the oral glucose tolerance test as a reference, offers an important note of caution. At the 6.5% threshold, HbA1c showed an estimated sensitivity of 51% and specificity of 96%; fasting glycemia at the 126 mg/dL threshold showed a sensitivity of 49% and specificity of 98%. Combining the two tests increased sensitivity to 64%, but the authors classified fasting glycemia as the single test with the best ability to confirm diabetes, based on its higher specificity and positive likelihood ratio [4].These results do not negate the complementarity described in the book, but they prevent interpreting HbA1c as an always preferable substitute for fasting glycemia. The conclusion also depends on the test chosen as a reference: in the original Palestinian study, the comparison was fasting glycemia; in the network meta-analysis, it was the oral glucose tolerance test. Furthermore, diagnostic performance changes with population, disease prevalence, red blood cell conditions, and laboratory procedures.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the study under review from the independent publications used to evaluate the narrative in the book's paragraph.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Diagnostic cross-sectional study	1,370 Palestinian Arab adults without known diabetes	HbA1c 6.3% best balance; HbA1c 6.5% more specific; low agreement in prediabetes	direct confirmation	moderate
[1]	Systematic review and meta-analysis	37 studies on adults without known diabetes	HbA1c 6.5%: sensitivity 50.0% and specificity 97.3%; estimated optimal threshold 6.03%	direct confirmation	high
[2]	Population-based cross-sectional observational study	3,523 Vietnamese adults aged 30 and older	Moderate agreement between HbA1c and fasting glycemia; greater discordance in prediabetes	direct confirmation	moderate
[3]	International pooled analysis of population studies	364,825 adults without known diabetes, 117 studies in 45 countries	Only 29-39% of cases identified at screening had both tests above threshold	indirect confirmation	high

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The analyzed study directly supports the idea that HbA1c and fasting glycemia provide complementary and not perfectly overlapping information. In the studied population, a lower HbA1c threshold increased the ability to identify individuals classified with diabetes by fasting glycemia, while the 6.5% threshold reduced false-positive classifications. Independent evidence strongly confirms this picture, especially for diabetes; for prediabetes, the discordance is greater, and interpretation requires further caution. The results do not justify considering a single test sufficient for every person or every population.

Aggiornato al 17/11/2026. Questo contenuto riflette una sintesi divulgativa delle evidenze scientifiche al momento della pubblicazione e non sostituisce il parere medico.

10. TRANSPARENCY AND SCIENTIFIC RESPONSIBILITY

Artificial Intelligence was used solely as a tool for editorial and documentary support. All content, interpretations, bibliographic citations and conclusions have been verified, reviewed and approved by the author, who assumes full scientific responsibility for them.

The manuscript was also subjected to independent peer review prior to publication.

To ensure the greatest transparency, the complete history of the article, including the dates of submission, revision, acceptance and publication, as well as information on the peer review process, is available on the dedicated Article History page.

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