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ORIGINAL RESEARCH

Glycated hemoglobin versus oral glucose tolerance test in identifying individuals with prediabetes in the Qatari population - A review of the evidence

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1. ABSTRACT

The study compared two methods for identifying prediabetes in 446 Qatari adults without known diabetes: glycated hemoglobin (HbA1c, an indicator of average blood sugar over the previous months) and the oral glucose tolerance test (OGTT, a test that measures the body's response to 75 grams of glucose). The two criteria showed low concordance. Individuals classified as having prediabetes only by the OGTT exhibited lower estimated pancreatic beta-cell function, a higher prevalence of metabolic syndrome, and a higher estimated future diabetes risk score compared to those identified only by HbA1c.In the narrative of “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, the study contributes to the passage stating that an isolated positive HbA1c result may not correspond to the same pathophysiological profile detected by an impaired glycemic response after a glucose load. Independent studies confirm that OGTT and HbA1c may select different groups and that the OGTT can detect alterations not captured by HbA1c. However, a large Chinese cohort shows that even elevated HbA1c with a normal OGTT can be associated with reduced beta-cell function. The most prudent conclusion is, therefore, that the tests describe different aspects of glucose regulation and that the clinical context and the population studied are decisive.

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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 and OGTT identified the same Qatari adults as having prediabetes and, crucially, whether the groups identified by the two tests had a comparable metabolic profile. The hypothesis was that the dynamic glucose tolerance test could recognize individuals with glucose regulation impairments not evident through the HbA1c value alone.The relevance to the "Choosing to Live in Health or Disease" section by Dr. A. Colonnese and R. Panzironi is specific: the publication does not demonstrate the entire natural history of diabetes, but it documents that, in this population, individuals positive only for HbA1c and those positive only for OGTT were not metabolically equivalent. The central point is the comparison between the function of pancreatic beta cells, which are the cells that produce insulin in response to glucose.As this is a cross-sectional study based on measurements collected at a single point in time, it can show differences between groups but cannot establish whether one test necessarily identifies an earlier or more advanced stage of the disease. Furthermore, the future risk of diabetes was not observed directly over time: it was estimated using a predictive model.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The authors performed a retrospective analysis of data collected during pre-employment health screenings at Qatar Petroleum. The study included 446 adults of Arab descent with no known diagnosis of type 2 diabetes, who were in good general health and not taking any medications known to alter glucose tolerance. Inclusion criteria required an HbA1c level below 6.5%, a fasting plasma glycemia below 126 mg/dl, and a two-hour glycemia below 200 mg/dl.All participants underwent a 75-gram OGTT after 10-12 hours of fasting. Glucose and insulin levels were measured while fasting and two hours after the load. HbA1c was measured using high-performance liquid chromatography, a laboratory technique used to quantify different forms of hemoglobin. Prediabetes according to OGTT was defined as a fasting glycemia between 100 and 125 mg/dl and/or a two-hour glycemia between 140 and 199 mg/dl. According to HbA1c, it was defined by values between 5.7% and 6.4%.Insulin sensitivity and beta-cell function were estimated using HOMA indices, which are calculations derived from fasting glycemia and insulin. Beta-cell function was expressed as the product of estimated insulin secretion and the reciprocal of insulin resistance. Metabolic syndrome was also identified according to ATP III criteria, and the 7-8 year diabetes risk was estimated using the Stern model. The exact data collection period is not reported in the available material. No prospective clinical follow-up is reported.

4. RESULTS

According to the OGTT, 296 out of 446 participants, or 66%, had prediabetes; 150, or 34%, had normal glucose tolerance. Using HbA1c instead, 200 people, or 45%, were classified as prediabetic and 246 as normoglycemic. Only 150 participants were classified as having prediabetes by both tests, and 100 as normal by both.In practice, 196 out of 446 people, or 44%, received conflicting classifications from the two methods. The kappa coefficient, an index that measures how much two classifications agree beyond chance, was 0.15 with P less than 0.0001: the concordance was statistically different from chance, but very low in practical terms. The correlations between HbA1c and fasting glycemia (r=0.16) and between HbA1c and two-hour glycemia (r=0.19) were also weak.The data most relevant to the book concerns the discordant groups. People with prediabetes according to the OGTT but with an HbA1c below 5.7% had an estimated beta-cell function of 34 ± 1, very close to that of the group positive by both criteria, which was 33 ± 1. People positive only for HbA1c had a beta-cell function of 51 ± 2, closer to the group normal by both tests, which was 55 ± 1. The overall difference between the four groups was statistically significant, with P less than 0.0001.The other indicators followed the same trend. The prevalence of metabolic syndrome was 62% in subjects positive only for the OGTT and 20% in subjects positive only for HbA1c. The Stern score, which estimates rather than directly measures the future probability of diabetes, was 16.1 ± 1 in the OGTT-only group and 19.8 ± 0.9 in the HbA1c-only group; both groups had values higher than the group normal by both criteria, which was 8.3 ± 0.6. However, the authors emphasize that this score does not replace the actual observation of diabetes incidence over time.

5. INTERPRETATION

In simple terms, the two tests do not capture the exact same aspect of metabolism. HbA1c summarizes average glucose exposure over time, while the OGTT observes how the body handles a rapid increase in glucose. A person can therefore have a normal average glycemia and, at the same time, an abnormal response after a glucose load.In the study analyzed, the segment actually documented is this: among Qatari adults, prediabetes defined solely by the OGTT was associated with lower estimated beta-cell function and a higher frequency of metabolic syndrome compared to prediabetes defined solely by HbA1c. The result supports the statement in the book that many subjects positive exclusively for HbA1c may present relatively preserved beta-cell function compared to those who show alterations in the OGTT.However, this observation does not justify considering HbA1c a useless test, nor does it prove that every subject with elevated HbA1c and a normal OGTT is metabolically healthy. HOMA indices are indirect estimates of beta-cell function, and the cross-sectional study does not demonstrate a causal sequence. Furthermore, the differences may depend on age, body composition, geographic origin, conditions that modify HbA1c, and the diagnostic thresholds used.

6. INDEPENDENT CONFIRMING EVIDENCE

An independent cohort of 522 Mexican-American adults provided confirmation that is particularly close to the passage discussed. All participants underwent a 75-gram OGTT and more detailed assessments of beta-cell function, based on insulin secretion and insulin sensitivity. In participants with normal glucose tolerance, beta-cell function was comparable both with HbA1c below 5.7% and with HbA1c between 5.7% and 6.4%. Conversely, the presence of impaired fasting glycemia or impaired glucose tolerance was associated with a marked reduction in beta-cell function, regardless of HbA1c levels. This separate cohort directly supports the idea that the impairment documented by the OGTT may identify a beta-cell defect that the HbA1c range alone does not fully describe [1]. The limitation is that this remains a cross-sectional analysis of a specific population.A retrospective study conducted in Thailand on 512 people at high metabolic risk confirmed that HbA1c and OGTT can classify different groups. The OGTT identified diabetes in 19.7% of participants, compared to 11.1% identified by HbA1c. For diabetes, an HbA1c of 6.5% or higher showed a sensitivity of 32% and a specificity of 94% compared to the OGTT; this means that the test was rarely positive in subjects without diabetes according to the adopted reference, but it failed to recognize a significant portion of subjects who were positive on the OGTT. Concordance for prediabetes was also low, with a kappa of 0.154 [2]. The study did not directly measure beta-cell function, so it confirms the diagnostic discordance but not the cellular mechanism observed in the Qatari population.In a cohort of 1,044 people without known diabetes undergoing coronary angiography, the combined use of HbA1c and OGTT revealed further differences in estimated beta-cell function. Among the 432 participants with a normal OGTT, an HbA1c of 42 mmol/mol or higher was associated with a lower HOMA-beta compared to an HbA1c below 42 mmol/mol: 107 ± 82 versus 132 ± 96, with P=0.018. Among the 423 participants with prediabetes according to the OGTT, an HbA1c of 48 mmol/mol or higher was associated with a lower HOMA-beta: 91 ± 52 versus 120 ± 88, with P=0.003 [3]. This study confirms that combining markers can describe different metabolic subgroups; however, it concerns patients with suspected or known coronary artery disease and cannot be automatically generalized to the entire population.

7. CONFLICTING EVIDENCE

Significant conflicting evidence comes from a Chinese cohort of 3,517 middle-aged or older individuals, all with normal glucose tolerance according to an OGTT. The authors compared 1,640 participants with an HbA1c of 5.7% or higher with 1,877 participants with an HbA1c below 5.7%. After statistical adjustments, the group with isolated elevated HbA1c maintained lower insulin sensitivity as assessed by the Matsuda index and a lower early disposition index, a measure of the beta cells' ability to compensate for insulin resistance [4].This result contrasts with the clearer interpretation that isolated HbA1c positivity generally indicates preserved beta-cell function. Instead, it shows that elevated HbA1c, even with a normal OGTT, can be associated with early metabolic impairment. The differences compared to the Qatari study may depend

on the population, age, selection criteria, the method used to estimate beta-cell function, and the fact that the Chinese cohort exclusively included people who were already normal according to the OGTT. No directly conflicting evidence sufficiently relevant to demonstrate the opposite of the discordance between HbAIc and OGTT has been identified; this does not prove the absence of contrary results.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the original study from independent research and shows that discordance between tests is repeatedly observed, while the pathophysiological significance of isolated elevated HbA1c varies across populations.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Retrospective cross-sectional observational	446 Qatari adults without known diabetes	OGTT-only prediabetes was associated with lower estimated beta-cell function and more frequent metabolic syndrome compared to HbA1c-only prediabetes.	direct confirmation	moderate
[1]	Cross-sectional observational	522 Mexican-American adults who underwent OGTT	IFG or IGT were associated with a marked reduction in beta-cell function independently of HbA1c; HbA1c 5.7-6.4% with normal OGTT did not show the same reduction.	direct confirmation	moderate
[2]	Retrospective cross-sectional observational	512 Thai patients at high metabolic risk	HbA1c and OGTT showed low concordance; HbA1c identified fewer cases of diabetes compared to OGTT.	indirect confirmation	moderate
[3]	Cross-sectional observational	1,044 patients without known diabetes who underwent coronary angiography	Adding HbA1c to OGTT distinguished subgroups with lower HOMA-beta.	biologically consistent evidence	moderate
[4]	Cross-sectional observational	3,517 Chinese adults with normal OGTT	Isolated elevated HbA1c was associated with lower insulin sensitivity and lower early beta-cell function.	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The study analyzed clearly shows that, in the observed Qatari population, HbA1c and OGTT were not interchangeable for identifying prediabetes. The group identified only by the OGTT showed lower estimated beta-cell function and a higher frequency of metabolic syndrome compared to the group positive only for HbA1c.Independent literature moderately confirms that the OGTT can detect alterations in glucose regulation and beta-cell function not fully represented by HbA1c. However, the apparently preserved beta-cell function in subjects with isolated elevated HbA1c is not a universal finding. The available evidence therefore supports an integrated and contextualized approach, without establishing that a single test is superior in every population or clinical circumstance.

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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