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ORIGINAL RESEARCH

Insulin resistance and beta-cell dysfunction in individuals with normal glucose tolerance but elevated plasma glucose one hour after a glucose load - A review of the evidence

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1. ABSTRACT

The analyzed study evaluated whether individuals considered normoglycemic by traditional criteria, but with elevated blood glucose one hour after an oral glucose load, already exhibit alterations in insulin metabolism. In 9,452 Chinese adults identified as being at risk for diabetes, the subgroup with a one-hour blood glucose level of 155 mg/dL or higher showed a marked reduction in early insulin secretion and the oral disposition index, an indicator of the pancreatic beta-cell capacity to compensate for insulin requirements.The research contributes to the narrative of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, according to which postprandial glycemic increase may appear before conventional diagnostic abnormalities and reflect early beta-cell deterioration. Independent studies, conducted in different populations and one with prospective observation, support this interpretation. However, it remains necessary to distinguish a metabolic risk indicator from a diagnosis of diabetes or proof of an individual causal relationship.

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MISSION

LIFE Science Hub – Journal of Science was founded with the aim of making scientific knowledge accessible without giving up methodological rigour, quality of sources and authoritativeness of content. The journal promotes the dissemination of knowledge in the health, nutrition, medical and longevity sciences, building a bridge between the world of research and society.

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 elevated plasma glycemia at one hour during an oral glucose tolerance test could identify metabolic alterations already present in people who maintained fasting glycemia and two-hour glycemia within the limits of normal glucose tolerance. The hypothesis was that a one-hour value equal to or greater than 8.6 mmol/L, or 155 mg/dL, was associated with both reduced insulin sensitivity and reduced pancreatic beta-cell function.Beta cells are the cells in the pancreas that release insulin when blood glucose increases. To maintain stable glycemia, it is not enough to produce insulin: it must be released rapidly and in quantities proportional to the tissues' sensitivity to the hormone. This balance is summarized by the disposition index, which combines insulin secretion and insulin sensitivity.The publication is relevant to two passages in "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi. In the chapter on postprandial glycemic variability, it is argued that, in apparently normoglycemic people, a high glycemic peak at one hour can be accompanied by an early loss of beta-cell function. In the chapter dedicated to beta-cell function, it is argued more specifically that early insulin secretion and the compensatory capacity of the pancreas can decrease more noticeably than insulin sensitivity.The study can document metabolic differences observed between groups classified based on the results of the same test. It cannot prove that high one-hour glycemia causes beta-cell dysfunction, nor can it establish whether every single person with that value will develop diabetes in the future.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

This is a retrospective study, meaning it is based on data previously collected. Researchers examined individuals predominantly of Han Chinese ethnicity who were considered by clinicians to be at risk for diabetes and who underwent a 75 g oral glucose tolerance test between July 1, 2010, and June 30, 2021.Of the 15,697 people initially evaluated, 9,452 were included. Exclusions included, among others, individuals with missing data, those under 18 years of age, pregnancy or gestational diabetes, type 1 diabetes, fasting glycemia below 2.8 mmol/L, values incompatible with the quality required for analysis, or values already within the diagnostic range for diabetes. The final population included 3,630 men and 5,822 women, with a median age of 54 years.After an overnight Fasting of 8-10 hours, glucose and insulin were measured while fasting and at 30, 60, and 120 minutes. Normal glucose tolerance was defined as fasting glycemia below 5.6 mmol/L and two-hour glycemia below 7.8 mmol/L. Within this group, the one-hour threshold was 8.6 mmol/L.Insulin sensitivity was estimated using the Matsuda index, a calculation derived from glucose and insulin values during the test: lower values indicate lower insulin sensitivity. Early insulin secretion was estimated using the 30-minute insulinogenic index, referred to as IGI30. Overall beta-cell function was represented by the oral disposition index, obtained by combining IGI30 and the Matsuda index. Since these are indirect indicators derived from the oral test and not measurements obtained using reference methods such as the clamp, they describe a physiological estimate rather than an absolute direct measurement.Continuous variables were compared using analysis of variance or the Kruskal-Wallis test, depending on the data distribution; categorical variables were compared using the chi-squared test. The analyses were two-tailed, and the significance level was set at P less than 0.05. No prospective follow-up is reported to verify the subsequent onset of diabetes.

4. RESULTS

According to the American Diabetes Association criteria, 3,577 participants, equal to 37.8% of the sample, had normal glucose tolerance. Among these, 1,403 people, or 39.2%, had a one-hour glycemia equal to or greater than 8.6 mmol/L. This subgroup was on average older: median age 53 years compared to 47 years in people with one-hour glycemia below the threshold.The most relevant result for the book's narrative concerns the initial insulin response. In people with normal glucose tolerance but high one-hour glycemia, the IGI30 was 11.79 versus 21.45 in the group with one-hour glycemia below 155 mg/dL. This is an approximate reduction of 45%, statistically significant with a P-value of less than 0.001. In simple terms, after the glucose load, the pancreas released less insulin in the first 30 minutes.The oral disposition index was also lower: 42.91 versus 91.4 in the group

with lower one-hour glycemia, a reduction of 53.05%, with a P-value of less than 0.001. Since this index considers both insulin secretion and tissue sensitivity to insulin simultaneously, the data indicates a lower capacity of beta cells to compensate for the metabolic load.Insulin sensitivity was also reduced, but to a lesser extent. The Matsuda index was 3.61 in the group with high one-hour glycemia and 4.64 in the group with a value below the threshold, with a P-value of less than 0.001. The authors interpreted this result as a 22.20% reduction. However, compared to groups with impaired fasting glucose or impaired glucose tolerance, the value in the normoglycemic group with high one-hour glycemia remained higher.The glucose and insulin curves showed another element consistent with a delayed pancreatic response: in the group with high one-hour glycemia, insulin at 30 minutes was lower, while levels at one and two hours were relatively higher. The profile resembled that of people with impaired fasting glucose. This does not directly prove the absence of the first-phase insulin response, which would require more specific tests, but it is compatible with a less efficient and more delayed early response.Using a disposition index of less than 48.50 as a reference, the authors calculated that the one-hour glycemia threshold of 8.6 mmol/L had a sensitivity of 94.60% for identifying severe impairment of estimated insulin secretion. The specificity was 69.50%. Since one-hour glycemia and the disposition index are both obtained from the same oral test data, this accuracy does not equate to external validation or definitive diagnostic capability in the general population.

5. INTERPRETATION

The main biological significance is that an apparently normal fasting and two-hour glycemia does not necessarily guarantee that the glucose response is fully efficient in the initial phases following a glucose load. In the sample examined, the elevated glycemic value at one hour was primarily associated with lower early insulin secretion and a reduction in calculated beta-cell function relative to insulin sensitivity.The chain segment documented by the analyzed study is therefore: elevated one-hour glycemia during an oral glucose tolerance test lower early insulin response lower oral disposition index. The reduction in insulin sensitivity was present, but quantitatively less marked than the reduction in insulin secretion and compensation indices.This interpretation is consistent with the passage from “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, which describes postprandial glycemia as a possible window into the early functional alterations of the pancreas. However, the data does not authorize the conclusion that beta-cell dysfunction always precedes insulin resistance in all populations. The observational design, the enrollment of individuals already considered at risk, and the use of indirect indices do not allow for the definition of a universal causal sequence.

6. INDEPENDENT SUPPORTING EVIDENCE

Independent physiological confirmation came from a study of 305 non-diabetic offspring of people with type 2 diabetes. Participants with normal glucose tolerance but a one-hour glycemia of 155 mg/dL or higher were compared with individuals whose one-hour glycemia was below that threshold. Insulin sensitivity was assessed using a hyperinsulinemic-euglycemic clamp, a technique that measures how much glucose the body uses when insulin is maintained at controlled levels. The group with high one-hour glycemia showed lower insulin sensitivity and, above all, a lower acute insulin response and a lower disposition index during an intravenous glucose test [1]. This study confirms with more direct methods the premise that an elevated one-hour value can identify a reduced compensatory capacity of beta cells. The limitation is that this comparison is also cross-sectional and does not demonstrate individual progression toward diabetes.In a Korean population, 192 people with normal glucose tolerance were divided based on their one-hour glycemia; they were also compared with 52 people with impaired glucose tolerance. Normoglycemic individuals with high one-hour glycemia had a mean oral disposition index of 1.8, compared to 3.5 in the group with low one-hour glycemia; the value was identical to that of the group with impaired glucose tolerance. The ISSI-2, an index that integrates insulin secretion and insulin sensitivity, was also reduced to 213.2 compared to 301.2 in the low one-hour glycemia group and was close to 172.5 in the group with impaired glucose tolerance [2]. This confirms the book's assertion that people not classified as prediabetic by conventional criteria may already

show beta-cell function similar to that observed in impaired glucose tolerance. However, the size of the subgroup with a high one-hour value was limited to 43 people.The link to future risk is supported by a Korean community cohort consisting of 5,703 people with normal glucose tolerance, followed for 12 years. During the follow-up, 593 participants, equal to 10.3%, developed diabetes. After adjustment for standard risk factors, a one-hour glycemia of 8.0 mmol/L or higher was associated with lower beta-cell function and a 2.84 times greater risk of incident diabetes compared to participants below that threshold [3]. The threshold analyzed does not coincide exactly with 155 mg/dL, and the study shows an association, not causality. However, it reinforces the prognostic part of the narrative: the one-hour glycemic value can signal metabolic risk before the conventional fasting or two-hour thresholds are exceeded.

7. CONFLICTING EVIDENCE

No directly conflicting evidence sufficiently relevant to the association between elevated one-hour glycemia and reduced beta-cell function has been identified; this does not prove the absence of contrary results.However, there is a significant difference in the insulin resistance component. In the Korean study that compared normal glucose tolerance with high or low one-hour glycemia, insulin sensitivity was described as comparable between the two subgroups, while beta-cell function was clearly reduced [2]. Conversely, the analyzed study and the clamp study also observed a reduction in insulin sensitivity [1]. This divergence does not contradict the core narrative regarding beta cells, but it suggests that the extent of insulin resistance associated with the one-hour value depends on population, body composition, ethnic characteristics, measurement method, and the stage of metabolic deterioration.Furthermore, the proposed thresholds are not uniform across studies. The prospective Korean work identified 8.0 mmol/L as a prognostic threshold, which is lower than 8.6 mmol/L [3]. Consequently, the value of 155 mg/dL is useful for describing the studied phenotype and for stratifying risk in specific contexts, but it should not be interpreted alone as a universal diagnosis or as a certainty of clinical progression.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication subject to the Evidence Review from the independent research used to verify the same narrative.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Retrospective cross-sectional observational	9,452 Chinese adults at risk for diabetes; 3,577 with normal glucose tolerance	One-hour glycemia ≥155 mg/dL associated with 45.03% reduced IGI30, 53.05% reduced oral disposition index, and lower insulin sensitivity	direct confirmation	moderate
[1]	Cross-sectional clinical study with clamp and intravenous test	305 non-diabetic offspring of people with type 2 diabetes	One-hour glycemia ≥155 mg/dL associated with lower insulin sensitivity, lower acute insulin response, and lower disposition index	direct confirmation	moderate
[2]	Cross-sectional observational	192 Koreans with normal glucose tolerance and 52 with impaired glucose tolerance	Beta-cell function adjusted for insulin sensitivity reduced in the group with high one-hour glycemia, to values similar to impaired glucose tolerance	direct confirmation	moderate
[3]	Prospective cohort	5,703 Koreans with normal glucose tolerance followed for 12 years	One-hour glycemia ≥8.0 mmol/L associated with lower beta-cell function and a 2.84 times higher risk of incident diabetes	indirect confirmation	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The study analyzed shows that, in individuals at risk for diabetes but still classified as normoglycemic based on fasting and two-hour values, a one-hour glycemia of 155 mg/dL or higher is associated with a marked reduction in early insulin secretion and estimated beta-cell function. This interpretation is confirmed by independent evidence, including research with more direct physiological measurements and a prospective cohort.

The narrative that postprandial glycemia can make early metabolic alterations visible is therefore well-supported. However, caution is needed when considering the 155 mg/dL threshold as an independent diagnostic criterion or when inferring an identical causal sequence for all individuals. The insulin resistance component appears to vary across

populations, while the most consistent signal concerns the deterioration of the compensatory capacity of beta cells.

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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