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The continuum of normal glucose tolerance in obese youth: evidence of beta-cell function impairment independent of insulin resistance - A review of the evidence

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1. ABSTRACT

The analyzed study evaluated 407 obese children, adolescents, and young adults with normal glucose tolerance to determine whether differences in blood glucose two hours after an oral glucose load were associated with variations in pancreatic beta-cell response. As the two-hour blood glucose level increased, while remaining below the diagnostic threshold for glucose intolerance, blood glucose rose more significantly in the first 30 minutes without a proportionate increase in insulin. This resulted in a reduction of the insulinogenic index, an estimate of early insulin response relative to the rise in glucose.The publication contributes to the passage from “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, which suggests that an impairment of the beta-cell response can be recognized even during normoglycemia and does not depend solely on insulin resistance. Independent studies using more direct measures of insulin sensitivity and insulin secretion confirm that, in young people who are overweight or obese, higher—yet still normal—post-load glycemic values are associated with lower pancreatic compensation. The evidence is consistent, but it primarily concerns selected populations and does not establish that a single glycemic value inevitably leads to diabetes.

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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 normal glucose tolerance truly represents a uniform condition in obese young people. In other words, the authors verified whether, even below the conventional threshold of 140 mg/dL two hours after an oral glucose load, relatively higher values were associated with a less effective response of pancreatic beta cells.The hypothesis was biologically plausible: when tissues respond less to insulin, the pancreas must increase insulin secretion to maintain glycemia within the normal range. To assess whether this adaptation is adequate, it is not enough to simply observe how much insulin is circulating in the blood; one must consider how much insulin is produced in relation to the increase in glucose and the degree of insulin sensitivity.The reason for the citation in the book's paragraph is specific. The research documents that, in normotolerant obese young people, higher glycemia two hours after the test was accompanied by a relatively less adequate early insulin response, even after stratification for insulin sensitivity. The study can therefore support the segment of the narrative regarding the early presence of reduced beta-cell reactivity. However, it cannot prove that such an alteration causes diabetes in every participant, nor can it define individual clinical outcomes over time.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The study had a cross-sectional observational design, meaning it compared measurements collected at a single point in time without following participants over time. 407 obese young people aged between 4 and 20 years with normal glucose tolerance underwent an oral glucose tolerance test, or OGTT (a test that measures how the body handles glucose after consuming a standardized amount).Participants were divided into three groups based on their two-hour plasma glycemia: less than 100 mg/dL, between 100 and 119 mg/dL, or between 120 and 139 mg/dL. The authors evaluated the change in glucose and insulin during the first 30 minutes of the OGTT. They also calculated the insulinogenic index, which is the ratio between the early increase in insulin and the increase in glucose: a lower value indicates that the insulin increase is less proportional to the glycemic stimulus.The analysis was repeated by stratifying participants by insulin sensitivity index, that is, by separating subjects with different tissue capacities to respond to insulin. This information is important because it allows for distinguishing, at least in part, a reduced pancreatic response from the mere presence of insulin resistance. Detailed inclusion and exclusion criteria, numerical distribution across the three groups, recruitment period, composition by sex and ethnicity, and mean values of the variables are not reported in the available material, which consists only of the abstract.

4. RESULTS

The main finding is that the initial glycemia after the load tended to rise more in groups with higher glycemia at two hours. Specifically, the increase in glucose between 0 and 30 minutes grew progressively as the two-hour glycemia increased, with statistical significance reported by the authors as $P < 0.05$. In simple terms, those who had a higher value at the second hour already showed a greater glycemic excursion in the first minutes of the test.The absolute increase in insulin between 0 and 30 minutes did not vary significantly between groups. However, since glucose increased more, the amount of insulin produced was not proportionally greater. The insulinogenic index decreased progressively as the two-hour glycemia increased, with $P < 0.02$. This finding does not necessarily mean that the pancreas was not producing insulin, but that its early response was relatively less effective compared to the glycemic load.The same trend for the insulinogenic index was observed at every level of insulin sensitivity, with $P < 0.02$. Furthermore, the insulin-glucose feedback system showed an unfavorable shift to the left as the two-hour glycemia increased, with $P < 0.005$. In practice, given the same metabolic context, higher post-load glycemia was associated with less favorable pancreatic compensation. The complete numerical data for each group, including means, standard deviations, and subgroup sizes, are not reported in the available material.

5. INTERPRETATION

To maintain normal glycemia, the pancreas must rapidly adjust insulin secretion to the amount of glucose entering the bloodstream. The publication

shows that, in the young obese individuals studied, this adjustment was less proportionate when the two-hour blood glucose level was closer to the upper limit of normal. The relevant finding for the book is therefore not the simple presence of insulin resistance, but the reduction in the early insulin response relative to the glycemic stimulus.The documented segment can be summarized as follows: higher glycemia during the OGTT, even within the normal range initial insulin response not proportionally increased lower insulinogenic index. Stratification by insulin sensitivity makes the interpretation consistent that the phenomenon does not depend solely on the different insulin resistance between the groups.However, an important distinction must be maintained. The cross-sectional design detects an association and does not demonstrate the temporal order of events. It therefore does not allow us to establish whether the reduced beta-cell reactivity always precedes the increase in glycemia, whether it is an initial consequence of it, or whether both reflect other metabolic factors. Furthermore, the insulinogenic index is an estimate obtained from the OGTT, not a direct measure of insulin secretion via a clamp.

6. INDEPENDENT SUPPORTING EVIDENCE

Particularly direct confirmation comes from Burns and colleagues, who studied 147 young people with overweight or obesity, aged between 8 and under 20, using both OGTT and euglycemic-hyperinsulinemic clamps and hyperglycemic clamps. Clamps are experimental tests that allow for a more controlled measurement of insulin sensitivity and insulin secretion. As the two-hour glycemia increased, both insulin sensitivity and the first phase of insulin secretion decreased. In subjects with two-hour glycemia between 120 and less than 140 mg/dL, still within normal glucose tolerance, the disposition index was approximately 40% lower compared to the group below 120 mg/dL. The disposition index combines insulin secretion and sensitivity and describes the compensatory capacity of the pancreas. This is a direct and methodologically more robust confirmation of the central step of the analyzed study, although it remains a cross-sectional comparison in a clinically selected population [1].Kim and colleagues added a longitudinal element in 233 obese Latino youths with a family history of type 2 diabetes. In this study, a one-hour OGTT glycemia equal to or greater than 155 mg/dL was associated with a greater deterioration of beta-cell function over time and, among those initially normotolerant, a 2.5 times higher probability of developing prediabetes during a follow-up of up to eight years. The observed signal was at one hour and not at two hours; therefore, it does not exactly replicate the parameter of the analyzed study. However, it confirms the broader pathophysiological step: a greater glycemic excursion during the load can identify less favorable beta-cell compensation even before diagnosable dysglycemia [2].In an independent sample of normotolerant obese children and adolescents, Olivieri and colleagues examined both the two-hour glycemia and the shape of the glycemic curve during the OGTT. Participants with two-hour glycemia between 120 and 139 mg/dL and a monophasic curve, i.e., without a second glucose drop-and-rise, did not differ from subjects with impaired glucose tolerance in terms of the Matsuda index and disposition index. The Matsuda index is an estimate of insulin sensitivity obtained from the OGTT. The result supports the idea that a portion of young people classified as normotolerant may present a metabolic profile similar to that of glucose intolerance. However, since the association depended on the combination of two indicators and the design was cross-sectional, this is a consistent but indirect confirmation of the relationship described by the original study [3].

7. CONFLICTING EVIDENCE

No directly conflicting evidence of sufficient relevance has been identified; this does not prove the absence of contradictory results. The main caveats stem rather from the fact that the available studies use different thresholds, different OGTT timings, and non-identical indices to estimate beta-cell function. Furthermore, some analyses show that the overall shape of the glycemic curve may add information beyond the two-hour glycemia alone [3].The literature therefore does not allow a single glycemic value within the normal range to be considered as an independent diagnostic proof of pancreatic dysfunction. The significance of the results depends on the context: age, degree of adiposity, puberty, ethnicity, family history of diabetes, insulin sensitivity, and the method used to estimate insulin secretion.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication subject to the review from the independent research used to evaluate the narrative of the paragraph.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Cross-sectional observational	407 obese youths, 4-20 years old, with normal glucose tolerance	Higher two-hour glycemia was associated with increased early glycemia without a proportional increase in insulin; insulinogenic index was reduced even at comparable levels of insulin sensitivity.	biologically consistent evidence	moderate
[1]	Cross-sectional observational with OGTT and clamp	147 youths with overweight or obesity, 8-	Between 120 and	direct confirmation	moderate
[2]	Prospective observational	233 obese Latino youths with a family history of type 2 diabetes	One-hour glycemia ≥155 mg/dL associated with a greater decline in beta-cell function and higher probability of prediabetes.	indirect confirmation	moderate
[3]	Cross-sectional observational	Obese children and adolescents with normal glucose tolerance	Two-hour glycemia of 120-139 mg/dL associated with an IGT-like profile when combined with a monophasic glycemic curve.	indirect confirmation	low

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The study analyzed clearly supports the idea that, in young people with obesity and normal glucose tolerance, higher two-hour glycemia values may be accompanied by a relatively insufficient early insulin response. This result is consistent with the concept that beta-cell function must be evaluated in relation to both glucose and insulin sensitivity.Independent evidence confirms quite well that reduced beta-cell compensation may be present before reaching diagnostic thresholds for prediabetes, especially in young people who are overweight or obese. It remains necessary to distinguish this pathophysiological finding from an individual prognosis: formally normal glycemia does not automatically equate to disease, nor does a single test allow for the determination of a person's future risk.

Aggiornato al 24/11/2026. 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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