LIFE Science Hub
JOURNAL OF SCIENCE
EXPANDING KNOWLEDGE ABOUT NUTRITION AND HEALTH

ORIGINAL RESEARCH
ISSN 2845-7501

Differential, weight-dependent contribution of insulin secretion and insulin clearance to obesity-related hyperinsulinemia - A review of the evidence

Dr.ssa M. Bitonti[1]

1 Nutritional Biologist, Italy

1. ABSTRACT

The analyzed study evaluated 291 individuals classified into five body mass index (BMI) groups to determine how much the increase in blood insulin depended on higher pancreatic secretion versus lower clearance, i.e., the reduced elimination of the hormone. In a fasting state, the increase in insulin was primarily driven by increased secretion. After a meal, however, the further increase in insulin in obese subjects was mainly attributed to reduced clearance. In parallel, the glycemic response after a meal was 38% to 82% higher as weight increased compared to normal-weight participants.The publication contributes to the passage in "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi, which states that as BMI increases, higher post-meal insulin may not fully compensate for reduced sensitivity to the hormone. Independent evidence confirms that reduced insulin clearance can contribute to hyperinsulinemia in obesity and insulin resistance. However, other studies show that in obese but metabolically healthier individuals, increased secretion may prevail without a measurable reduction in clearance. The conclusion is therefore moderate and dependent on the metabolic context.

ONLINE ARTICLE

ARTICLE INFORMATION

Published: November 18, 2026
Updated: November 18, 2026

DOI 10.5281/zenodo.24338687

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 hyperinsulinemia associated with excess weight—that is, a high concentration of insulin in the blood—stems primarily from increased pancreatic production or decreased clearance of the hormone. This distinction is important: the amount of circulating insulin is the result of the balance between what the pancreas secretes and what the liver, in particular, removes from circulation.The hypothesis evaluated was that the relative contribution of insulin secretion and clearance changes when moving from normal weight to overweight and obesity, particularly after a meal. The study is relevant to paragraph 3.4 because it documents the final segment of the narrative: with a higher BMI, postprandial insulin can increase while glycemic control worsens, suggesting incomplete metabolic compensation.The research observes differences between BMI groups and does not randomly assign weight gain or experimentally modify clearance. It can therefore show how secretion, clearance, insulin, and glycemia are distributed across the studied groups, but it cannot demonstrate that reduced clearance is the sole cause of lower insulin sensitivity or the future onset of type 2 diabetes.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

Only the abstract is available. The study included 291 subjects, divided into five subgroups according to the World Health Organization weight classes based on BMI. The abstract reports BMI groups of 25, 30, 35, and 40, in addition to the normal-weight group, but does not report the size of each subgroup, age, sex, geographic or ethnic origin, recruitment period, or inclusion and exclusion criteria.Fasting and post-meal concentrations of insulin, C-peptide, and glucose were evaluated. C-peptide is a substance released along with insulin by the pancreas and helps to estimate how much hormone has actually been secreted. The authors also estimated insulin secretion and insulin clearance. The calculation formulas, type of meal, sampling times, laboratory techniques, statistical procedures, and any adjustments for confounding factors are not reported in the available material.No clinical endpoints, follow-up period, or therapeutic interventions are reported. This is therefore a physiological and metabolic comparison between weight categories, useful for describing plausible mechanisms but not for estimating individual prognoses.

4. RESULTS

In a fasting state, as BMI increased, insulin concentrations rose progressively and in a statistically significant manner. The same trend was observed for C-peptide and estimated insulin secretion. This means that, in the basal state, the pancreas contributed significantly to the increase in circulating insulin. Conversely, the reduction in clearance was less closely linked to BMI than secretion was.Fasting glycemia did not change in the group with a BMI of 25, whereas in the groups with a BMI of 30, 35, and 40, it was approximately 8% higher compared to those of normal weight. This increase, even without absolute values reported in the abstract, indicates that fasting glycemic balance was already less favorable in the groups with obesity.After a meal, insulin concentrations were significantly higher in the overweight and obese groups compared to the normal-weight group. However, the relationship with BMI was less clear than that observed during fasting. Postprandial insulin secretion increased in the overweight group but did not increase further in the obese groups. In those with obesity, therefore, the subsequent rise in circulating insulin was attributed by the authors primarily to a reduction in insulin clearance, rather than a further increase in secretion.The result most relevant to the book's paragraph concerns postprandial glycemia: its response was 38% to 82% higher in groups with increasing weight compared to those of normal weight. In simple terms, higher insulin was not accompanied by equally effective glycemic control. The abstract does not report absolute values, confidence intervals, specific P-values for individual comparisons, or direct measures of insulin sensitivity.

5. INTERPRETATION

The core finding suggests that hyperinsulinemia does not have a single biological meaning. In the fasting state, across all participants, the increase in insulin was primarily associated with greater pancreatic secretion. After a meal, however, in participants with obesity, the higher presence of insulin in the blood

appeared to depend increasingly on the fact that the hormone was being cleared more slowly.For the reader, the important point is that having high levels of insulin in the blood is not automatically equivalent to producing a large amount of it. If the liver and other tissues eliminate it less rapidly, peripheral concentration can increase even without a proportional increase in secretion. C-peptide allows these two processes to be partially separated, because it reflects pancreatic secretion without being cleared by the liver in the same way as insulin.In paragraph 3.4, the publication supports the following sequence: higher BMI lower postprandial clearance in obese individuals higher circulating insulin without a further increase in secretion higher postprandial glycemia. The observed data alone does not prove that reduced clearance causes insulin resistance, nor that high insulin is ineffective in every obese person. However, it shows that, in this population, the increase in insulin after a meal did not prevent a parallel worsening of the glycemic response.

6. INDEPENDENT SUPPORTING EVIDENCE

A 2022 study examined two independent cohorts: 460 participants evaluated with an oral glucose tolerance test and 81 who also underwent an intravenous test and a hyperinsulinemic-euglycemic clamp, a procedure that measures insulin sensitivity with greater precision. All obese participants without diabetes showed reduced insulin clearance; the reduction became more pronounced as insulin resistance increased. In the early stages of metabolic impairment, secretion did not increase correspondingly. This directly confirms the part of the narrative suggesting that lower insulin clearance can contribute to the hyperinsulinemia of obesity, although it remains an observational study and not a causal demonstration [1].An analysis of 470 Mexican-American adults showed that fasting insulin was independently dependent on metabolic insulin clearance, insulin sensitivity, BMI, waist circumference, and fasting glycemia. In the multivariate model, lower clearance and lower sensitivity were associated with higher insulin, while higher BMI, waist circumference, and glycemia were also associated with higher insulin. This evidence does not directly concern the postprandial period, but it supports an essential step in the narrative: the value of insulin in the blood cannot be interpreted as an indicator of pancreatic secretion alone [2].In a metabolic study of 92 people without diabetes, compared across groups of insulin-sensitive overweight, insulin-sensitive obese, and insulin-resistant obese individuals, the insulin-resistant obese people had the largest areas under the curve for glucose, insulin, and insulin secretion, and the lowest clearance. Compared to insulin-sensitive obese individuals, the reduction in clearance appeared in the group with insulin resistance. The work therefore confirms that both secretion and clearance contribute to hyperinsulinemia, but in different proportions depending on the metabolic context [3].

7. CONFLICTING EVIDENCE

An important element of caution comes from a physiological study that compared eight lean adults and eight adults with obesity, selected for having similar multi-organ insulin sensitivity. After glucose ingestion, insulin secretion was 50% to 100% higher in the group with obesity, while insulin clearance did not differ between groups. In six women with obesity, an average weight loss of 19% reduced basal and early post-glucose secretion even without an improvement in insulin sensitivity. This result is discordant with the idea that lower clearance is always the main explanation for postprandial hyperinsulinemia in obesity [4].The discrepancy does not invalidate the result of the original study. Instead, it indicates that the contribution of clearance depends on the population composition, the degree of insulin resistance, the presence of glycemia alterations, and the method used to estimate insulin kinetics. The discordant study had a very small sample size and included metabolically selected obese individuals; therefore, it cannot establish which mechanism prevails in the general population.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication covered in the review from independent research that confirms or defines the scope of the book's narrative.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Cross-sectional physiological observational	291 subjects across five BMI classes	In obese individuals, further postprandial hyperinsulinemia was primarily attributed to reduced clearance; postprandial glycemia increased with BMI.	direct confirmation	moderate
[1]	Observational with metabolic tests	Two cohorts: 460 and 81 participants; obese subjects without diabetes included	Insulin clearance was reduced in all obese participants and worsened with insulin resistance; initial secretion did not increase in parallel.	direct confirmation	moderate
[2]	Cross-sectional observational	470 Mexican-American adults	Lower metabolic insulin clearance was independently associated with higher fasting insulin.	indirect confirmation	moderate
[3]	Observational metabolic study	92 adults without diabetes, overweight or obese	In the insulin-resistant obese group, higher secretion, higher glycemic response, and lower clearance coexisted.	biologically consistent evidence	moderate
[4]	Controlled physiological study	8 lean adults, 8 with obesity; substudy in 6 women with obesity	In insulin-sensitive obesity, postprandial secretion was higher, while clearance did not differ from the lean group.	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The study analyzed clearly supports the idea that, in obesity, post-meal insulin concentration may increase due to a reduced clearance of the hormone. The simultaneous worsening of postprandial glycemia indicates that higher insulin levels do not guarantee complete metabolic compensation. Independent research moderately confirms the role of reduced clearance, but shows that the relative weight of secretion and removal varies with insulin resistance, population composition, and assessment method. Therefore, it is incorrect to interpret every case of hyperinsulinemia as proof of pancreatic hypersecretion or to attribute a universal causal role to clearance.

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.

11. RIFERIMENTI BIBLIOGRAFICI

[1] **Impaired Insulin Clearance as the Initial Regulator of Obesity-Associated Hyperinsulinemia: Novel Insight Into the Underlying Mechanism Based on Serum Bile Acid Profiles**
Fu et al., 2022
Diabetes Care
DOI: https://doi.org/10.2337/dc21-1023

[2] **Fasting insulin reflects heterogeneous physiological processes: role of insulin clearance**
Goodarzi et al., 2011
American Journal of Physiology-Endocrinology and Metabolism
DOI: https://doi.org/10.1152/ajpendo.00013.2011

[3] **Dissecting the relationship between obesity and hyperinsulinemia: Role of insulin secretion and insulin clearance**
Kim et al., 2017
Obesity
DOI: https://doi.org/10.1002/oby.21699

[4] **Obesity Is Associated With Increased Basal and Postprandial b-Cell Insulin Secretion Even in the Absence of Insulin Resistance**
van Vliet et al., 2020
Diabetes
DOI: https://doi.org/10.2337/db20-0377