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

ORIGINAL RESEARCH

Hyperinsulinism and Polycystic Ovary Syndrome (PCOS): The role of insulin clearance - Evidence review

Dott. A. Conte[1]

1 Nutritional Biologist, Italy

1. ABSTRACT

The analyzed study compared 22 women with polycystic ovary syndrome (PCOS) and normal glucose tolerance with 21 women with prediabetes, matched for age and body mass index. Using a hyperinsulinemic-euglycemic clamp and an oral glucose tolerance test, the authors observed similar peripheral insulin sensitivity in both groups, but lower metabolic insulin clearance in women with PCOS and an inverse relationship between clearance and insulin levels after glucose intake.The publication contributes to the passage from “The Choice to Live in Health or Illness” by Dr. A. Colonnese and R. Panzironi, which states that excess circulating insulin in PCOS does not depend exclusively on increased pancreatic secretion, but also on reduced elimination of the hormone. Independent studies confirm that reduced clearance is frequent in PCOS, although it shows heterogeneity linked to obesity, androgens, and clinical phenotype. The most prudent conclusion is that reduced clearance contributes to hyperinsulinemia in many, but not necessarily all, women with PCOS.

ONLINE ARTICLE

ARTICLE INFORMATION

Published: November 17, 2026
Updated: November 17, 2026

DOI 10.5281/zenodo.24304608

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—that is, the presence of high concentrations of insulin in the blood—in women with PCOS depends solely on a reduced tissue response to the hormone or also on its decreased elimination. The hypothesis was that women with PCOS and normal glycemia might have an insulin action profile similar to that of women with prediabetes who are comparable in age and body mass index, but differ in the way insulin is cleared from circulation.The connection to section 3.3 of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi is precise: the study examines whether elevated insulin in PCOS may reflect reduced metabolic clearance, in addition to pancreatic secretion. Clearance is the rate at which the body removes insulin from the blood; the liver plays a central role in this process, but the measurement taken during the clamp also includes the peripheral removal of the hormone.The study can therefore document a difference between groups and an inverse association between clearance and circulating insulin. However, it cannot establish the cause of the reduced clearance, nor can it demonstrate that it is the sole origin of hyperinsulinemia or that it necessarily precedes insulin resistance in PCOS.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The available material is only the abstract. The study included 22 women with PCOS and normal glucose tolerance and 21 women with prediabetes without hyperandrogenism or ovulatory disorders, matched for age and body mass index. Hyperandrogenism indicates increased levels or effects of androgens, sex hormones also present in women.All participants underwent a hyperinsulinemic-euglycemic clamp, an experimental procedure in which insulin is infused and glucose is kept stable to estimate how much glucose the body uses in response to the hormone. Insulin sensitivity was assessed using the M-value, which is the amount of glucose required to maintain stable glycemia during the clamp. An oral glucose tolerance test (OGTT) was also performed, with measurements taken after glucose intake.Insulin secretion was estimated using the insulinogenic index, the oral disposition index, and the area under the curve for insulin over two hours. Clearance was estimated as the metabolic insulin clearance rate during the clamp. Complete inclusion and exclusion criteria, recruitment period, detailed clinical characteristics, infusion dosages, complete statistical methods, and study location are not reported in the available material.

4. RESULTS

In simple terms, women with PCOS had a higher insulin response after a glucose load, but did not show peripheral insulin sensitivity different from that of women with prediabetes of the same weight and age. The two-hour insulin area under the curve, which summarizes insulin exposure after the test, was greater in PCOS ($p<0.011$). The insulinogenic index and the oral disposition index were also higher, with $p<0.001$ respectively.Overall two-hour glycemia was lower in the PCOS group, with a statistically significant difference. The M-value did not differ between the groups; therefore, no measurable difference in peripheral insulin sensitivity between PCOS and prediabetes emerged in this sample.The most relevant result for the book concerns clearance. The metabolic insulin clearance rate was lower in women with PCOS: median 420 $ml/m^2/min$, interquartile range 227-588, compared to 743 $ml/m^2/min$, interquartile range 597-888, in women with prediabetes ($p<0.001$). This means that, during the clamp, insulin was removed from the blood more slowly in the PCOS group.In the PCOS group, lower clearance was independently associated with a greater area under the insulin curve after glucose: coefficient $b=-0.878$, $p<0.001$. The association was also inverse in the prediabetes group, $b=-0.501$. A negative coefficient here indicates that as clearance decreased, insulin exposure increased. This data shows a strong relationship, but does not by itself prove a causal link.

5. INTERPRETATION

The primary biological significance is that the concentration of insulin in the blood does not depend solely on how much insulin is produced by the pancreas. It also depends on how quickly the body eliminates it. If removal slows down, the same secreted amount can remain in circulation longer and produce higher blood levels.In the comparison

performed, PCOS was distinguished from prediabetes primarily by lower clearance and greater insulin exposure, rather than a difference in the M-value. The segment of the chain documented by the publication subject to the Evidence Review is therefore: PCOS with normal glucose tolerance reduced metabolic insulin clearance higher hyperinsulinemia during the OGTT.The authors interpret the reduced clearance as a major contributor to hyperinsulinemia in PCOS. This is an interpretation consistent with the observed correlation, but the cross-sectional design does not allow for the complete separation of the roles of clearance, secretion, adiposity, androgens, and other metabolic factors. Furthermore, the clearance measured during the clamp is not equivalent to a direct measurement of hepatic insulin extraction alone.

6. INDEPENDENT SUPPORTING EVIDENCE

Independent confirmation comes from a study of 35 women with PCOS and 10 normo-ovulatory controls. The participants underwent an OGTT and a hyperinsulinemic-euglycemic clamp. Hyperinsulinemic women with PCOS showed lower hepatic insulin clearance values compared to both the controls and the normoinsulinemic women with PCOS, regardless of body mass index. The study directly supports the premise that reduced insulin clearance may contribute to hyperinsulinemia in PCOS; however, the sample size was small, and the subgroups were further divided by weight and insulin level [1].A second, larger study evaluated 190 women with PCOS and normal glucose tolerance using a hyperinsulinemic-euglycemic clamp. Metabolic insulin clearance was reduced in approximately two-thirds of the participants. In multivariate analysis, adiposity, estimates of insulin secretion, and androgen concentrations were independent predictors of clearance. This evidence confirms the direction of the association observed in the analyzed study and adds that the phenomenon is not uniform: reduced clearance is also linked to the individual woman's body composition and hormonal characteristics [2].Taken together, these studies do not show that pancreatic secretion is irrelevant. Instead, they show that hyperinsulinemia can arise from a combination of two components: increased secretion and decreased removal. This is precisely the specific point in the book's narrative to which the original publication contributes.

7. CONFLICTING EVIDENCE

A result useful for defining the limits of generalization comes from a study that compared 15 lean women with PCOS and 28 obese women with PCOS with their respective control groups. In lean women with PCOS, no significant differences emerged compared to lean controls regarding early insulin secretion, C-peptide, or hepatic insulin extraction. In obese women with PCOS, however, post-glucose insulin was higher, and early C-peptide secretion did not increase in parallel; hepatic extraction was only slightly and not significantly reduced compared to obese controls [3].These data do not directly refute the analyzed study, but they indicate that reduced clearance cannot be demonstrated with the same evidence in every PCOS phenotype. Abdominal obesity, fat distribution, diagnostic criteria, method of clearance estimation, and subgroup size can alter the results. No directly conflicting evidence sufficiently relevant to demonstrate an increase in clearance in PCOS has been identified; this does not prove the absence of contrary results.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the study covered in the review from independent publications and summarizes the level at which each piece of evidence contributes to the narrative.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Comparative observational with clamp and OGTT	22 normoglycemic women with PCOS and 21 women with prediabetes, matched for age and body mass index	In PCOS, lower metabolic insulin clearance and greater insulin exposure; peripheral sensitivity similar to the prediabetes group	direct confirmation	moderate
[1]	Experimental observational with OGTT and clamp	35 women with PCOS and 10 normo-ovulatory controls	Hyperinsulinemic women with PCOS had lower hepatic clearance compared to controls and normoinsulinemic PCOS	direct confirmation	moderate
[2]	Observational with clamp	190 women with PCOS and normal glucose tolerance	Reduced metabolic clearance in approximately two-thirds of participants; adiposity, secretion, and androgens were independent predictors	direct confirmation	moderate
[3]	Comparative observational with OGTT and clamp	15 lean and 28 obese women with PCOS, with 34 controls stratified by weight	In lean women, no significant differences in hepatic extraction emerged; results varied with obesity	discordant evidence	low

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The analyzed study appropriately supports the idea that hyperinsulinemia in PCOS should not be interpreted solely as the result of increased pancreatic secretion. In participants with PCOS, metabolic insulin clearance was lower compared to the prediabetes group matched for age and weight, and was associated with a greater insulin response following glucose intake.Independent evidence confirms that reduced clearance frequently contributes to hyperinsulinemia in PCOS. However, the phenomenon appears heterogeneous and dependent on the clinical context, particularly on adiposity, androgen profile, and individual metabolic characteristics. The book's narrative is therefore moderately supported regarding the specific passage on the contribution of reduced insulin elimination, while the causes and temporal sequence of the phenomenon require further validation.

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.

11. RIFERIMENTI BIBLIOGRAFICI

[1] **Heterogeneity in beta cell activity, hepatic insulin clearance and peripheral insulin sensitivity in women with polycystic ovary syndrome**
Ciampelli et al., 1997
Human Reproduction
DOI: https://doi.org/10.1093/humrep/12.9.1897

[2] **Serum Androgens Are Independent Predictors of Insulin Clearance but Not of Insulin Secretion in Women With PCOS**
Tosi et al., 2020
The Journal of Clinical Endocrinology & Metabolism
DOI: https://doi.org/10.1210/clinem/dgaa095

[3] **Insulin sensitivity, insulin secretion, and metabolic and hormonal parameters in healthy women and women with polycystic ovarian syndrome**
Morin-Papunen et al., 2000
Human Reproduction
DOI: https://doi.org/10.1093/humrep/15.6.1266