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ORIGINAL RESEARCH

Pathophysiology of type 2 diabetes in sub-Saharan Africans - Evidence review

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1. ABSTRACT

The analyzed study is a narrative review examining the mechanisms of type 2 diabetes in sub-Saharan African populations. The authors propose that hyperinsulinemia, i.e., a persistently high concentration of insulin in the blood, may result from both increased pancreatic secretion and reduced hepatic clearance, the process by which the liver, in particular, removes insulin from circulation.The publication contributes to the section of "The Choice to Live in Health or Illness" by Dr. A. Colonnese and R. Panzironi dedicated to metabolic differences between populations. Independent literature shows that people of West African or African ancestry may present higher insulin levels and lower insulin clearance compared to European groups. An important prospective study, in a different population, has also associated lower clearance with a higher incidence of diabetes. However, differences between studies, the observational nature of much of the evidence, and the limited availability of longitudinal data in sub-Saharan Africa require caution in defining a universal causal sequence.

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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 central question of the publication is whether the biological sequence leading to type 2 diabetes in Black African populations is always comparable to the traditional model built primarily on populations of European descent. In that model, insulin resistance—that is, the reduced ability of tissues to respond to insulin—is considered the initial defect; the pancreas would then increase insulin secretion as a compensation, until the progressive deterioration of beta cells occurs.The authors discuss a different hypothesis: in a portion of sub-Saharan African populations, hyperinsulinemia may appear early and be sustained by two components. The first is increased insulin secretion. The second is reduced hepatic clearance, meaning a lower removal rate of the hormone during its first pass through the liver. This is the segment relevant to the book's paragraph: the concentration of insulin in the blood depends not only on how much the pancreas produces, but also on how quickly the body eliminates it.The publication is a narrative review, not a clinical study that directly enrolls new participants. It can therefore bring together previous results, highlight convergences, and formulate a pathophysiological model. However, it cannot prove on its own that reduced clearance causes diabetes, nor can it establish that the same order of events applies to every person, sex, territory, or group of African ancestry.

3. MATERIALS AND METHODS OF THE ORIGINAL STUDY

The authors conducted a review of the scientific literature regarding the pathophysiology of type 2 diabetes in sub-Saharan African populations, including comparisons with people of African descent living in other countries. The text examines cross-sectional studies—snapshots of a single moment in time—as well as observational studies, research on body composition, adipose tissue metabolism, beta-cell function, and lifestyle interventions.The review distinguishes the contribution of insulin secretion from that of insulin clearance using, among other elements, data on insulin and C-peptide. C-peptide is released by the pancreas along with insulin but is primarily eliminated by the kidneys; comparing it with insulin can help to indirectly separate pancreatic production from the hepatic removal of the hormone.A systematic literature search protocol is not described, including databases queried, search dates, formal inclusion criteria, risk of bias assessment, or quantitative meta-analysis. This information is not reported in the available material. It is noted that the authors also consider preliminary, unpublished analyses of a prospective cohort of 112 Black South African women with normal glucose tolerance, followed for 1.5 years.

4. RESULTS

The main narrative finding is that, compared to white European individuals, many Black African populations or those in the diaspora more frequently exhibit hyperinsulinemia despite having similar glucose tolerance. The authors report that this clinical picture is characterized by higher insulin secretion, lower hepatic clearance, or a combination of both conditions. The practical implication is that a high blood insulin level does not automatically indicate that the pancreas is necessarily producing a proportionally high amount of the hormone.The review highlights that many of the available studies are cross-sectional. These studies document that insulinemia, secretion, clearance, and insulin sensitivity can coexist differently across population groups, but they do not establish which alteration appeared first. The authors cite findings from West Africa, the United Kingdom, and the United States indicating that reduced hepatic clearance is a significant contributor to hyperinsulinemia in adults of African descent.However, the publication also reports data that are not entirely consistent. In Black South African women with obesity, the authors observed that elevated insulin secretion was more closely associated with hyperinsulinemia than reduced clearance. Furthermore, in preliminary, unpublished analyses of a cohort of 112 women, secretion—rather than clearance—predicted the onset of dysglycemia after 1.5 years. Since these latter results are not presented as a full peer-reviewed publication, they do not allow for detailed independent verification.The authors therefore propose a hypothetical chain of events: hyperinsulinemia favored by hypersecretion and reduced hepatic clearance, followed by an increase in adiposity and a reduction in insulin sensitivity, with subsequent

overload and possible failure of beta cells. The text clarifies that this model requires confirmation through longitudinal and interventional studies.

5. INTERPRETATION

For the reader, the essential point is that the liver is not merely an organ that disposes of excess insulin. Since it is the first to receive insulin secreted by the pancreas, it can modulate the amount of the hormone that reaches the muscles, adipose tissue, and other organs. If insulin clearance decreases, peripheral exposure to insulin can increase even with the same level of secretion.This passage aligns with the book's narrative regarding metabolic differences between ethnic groups: reduced insulin clearance may help explain part of the hyperinsulinemia observed in some populations of African descent. The study analyzed does not correctly state that clearance is the sole determinant. Instead, it describes a balance between pancreatic secretion, hepatic elimination, adiposity, fat distribution, insulin sensitivity, sex, environment, and social context.The hypothesis that reduced clearance precedes insulin resistance is biologically plausible, but it requires a rigorous distinction. An association between low clearance and insulin resistance may also reflect a compensatory adaptation of the body or common factors, such as adiposity and liver function. To demonstrate a causal relationship, repeated measurements over time are needed, and ideally, interventions capable of selectively modifying clearance to observe the metabolic consequences.

6. INDEPENDENT SUPPORTING EVIDENCE

Direct confirmation of the ethnic component of this narrative comes from a comparative study conducted on individuals with normal glucose tolerance. Osei and colleagues compared native Ghanaians, Ghanaian immigrants, African Americans, and white Americans following a 75 g oral glucose load. In the three groups of West African ancestry, fasting and post-glucose insulin levels were higher compared to the white group, while post-meal C-peptide concentrations did not differ significantly. Hepatic extraction and insulin clearance were reduced by 25% to 52% in the groups of West African ancestry. This finding confirms that lower insulin elimination can contribute to hyperinsulinemia without necessarily implying higher secretion measurable via C-peptide [1]. The main limitation is the cross-sectional design, which does not allow for determining whether low clearance precedes insulin resistance or diabetes.A second independent study examined 40 Black African men and 41 white European men, with either normal glucose tolerance or type 2 diabetes. Endogenous insulin clearance was estimated during a mixed-meal test using C-peptide modeling; insulin sensitivity was measured using a hyperinsulinemic-euglycemic clamp, an experimental procedure that quantifies how much glucose the body can utilize under insulin stimulation. Black African men showed significantly lower clearance compared to white European men. In a multivariate analysis, ethnicity, insulin sensitivity, and adiponectin were independent predictors of clearance; age, visceral fat, and TNF-alpha did not contribute significantly [2]. This supports the premise that clearance can provide information beyond just adiposity or insulin resistance alone. However, the sample was small, composed exclusively of men, and does not allow for causal inferences.The link to diabetes susceptibility is supported, in a different population, by a longitudinal cohort of 570 Native American adults without diabetes. Of these, 448 were followed for a median of 7.9 years, and 146, or 32%, developed diabetes. Lower metabolic insulin clearance was associated with a higher percentage of body fat, higher fasting insulin, a greater acute insulin response, and lower insulin sensitivity. After adjusting for these factors and baseline glycemia, each higher standard deviation of clearance was associated with a lower risk of incident diabetes, with a hazard ratio of 0.77; 95% confidence interval from 0.61 to 0.98; P=0.03 [3]. In simple terms, higher clearance was associated with a lower probability of developing diabetes during follow-up. The study reinforces the prognostic importance of clearance, but it does not prove that reducing it causes diabetes and cannot be automatically transferred to sub-Saharan African populations.

7. CONFLICTING EVIDENCE

Important contextual evidence comes from the Insulin Resistance Atherosclerosis Study, which evaluated 1,295 participants of diverse ethnic backgrounds using frequently sampled intravenous glucose tolerance tests. Metabolic insulin clearance was lower in African Americans and Hispanics compared to non-Hispanic whites. However, the authors concluded that these

differences were largely explained by adiposity, insulin sensitivity, and acute secretory response [4].This finding does not deny that lower clearance may contribute to hyperinsulinemia. It does, however, show that its significance may depend on the measurement method, population composition, and the relationship with other metabolic factors. In particular, it reduces the strength of the hypothesis that clearance is always an independent trait or the initial event in the pathological sequence. No sufficiently relevant directly conflicting evidence has been identified that demonstrates the absence of reduced clearance in sub-Saharan African populations; this does not prove the absence of contrary results.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

The table distinguishes the publication under review from the independent research used to evaluate the book's narrative passage.

Quadro comparativo

Reference	Study type	Population or model	Main result	Direction of evidence	Strength of evidence
Original study	Narrative review	Studies on sub-Saharan African populations and the African diaspora	Proposes that hyperinsulinemia, high secretion, and reduced hepatic insulin clearance may contribute to the pathophysiology of diabetes.	biologically consistent evidence	moderate
[1]	Cross-sectional comparative observational	Native Ghanaians, Ghanaian immigrants, African Americans, and white Americans with normal glucose tolerance	Groups of West African ancestry had higher insulin levels and 25% to 52% lower insulin clearance compared to white Americans.	direct confirmation	moderate
[2]	Cross-sectional comparative observational	81 Black African or white European men, with normal glucose tolerance or type 2 diabetes	Black African men had lower insulin clearance; ethnicity, insulin sensitivity, and adiponectin were independent predictors.	direct confirmation	moderate
[3]	Prospective observational cohort	570 Native American adults without diabetes; 448 followed for a median of 7.9 years	Higher clearance was associated with a lower risk of incident diabetes after adjustment for metabolic factors.	indirect confirmation	moderate

[4]	Multicenter cross-sectional observational	1,295 participants from the Insulin Resistance Atherosclerosis Study	Ethnic differences in clearance were largely explained by adiposity, insulin sensitivity, and secretion.	discordant evidence	moderate

9. SINTESI EDITORIALE E CONCLUSIONI

CONCLUSIONS

The analyzed publication provides relevant support for the book's claim that insulin clearance contributes to the hormone's concentration in the blood and may help explain certain metabolic differences observed between populations. Independent studies confirm that groups of African ancestry may exhibit lower insulin clearance and higher insulinemia compared to European groups.It is moderately supported that reduced clearance is a factor associated with susceptibility to diabetes. However, it remains to be validated, especially through longitudinal studies in sub-Saharan Africa, whether this is the initial and causally determining event of insulin resistance or type 2 diabetes. Therefore, insulin concentration should not be interpreted as an exclusive indicator of beta-cell function.

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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