

How Research About Insulin Resistance Concerning Polycystic Ovary Syndrom Inform Reproductive Health Promotion?

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29 October 2023

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Introduction

Polycystic Ovary Syndrome (PCOS) stands as a multifaceted endocrine disorder, generally affecting women of reproductive age. PCOS is characterised by a range of symptoms, like ovarian dysfunction and infertility, and correlates with metabolic abnormalities like Insulin Resistance (IR). The intersection of these symptoms not only impacts the immediate reproductive health of women but is also associated with long-term metabolic risks. This academic report delves into the problem of IR concerning PCOS and explores how this relationship informs and shapes reproductive health promotion and disease prevention strategies.

The report systematically explores this question through the following sections:

- Background: provides an overview of PCOS and IR, establishing the topic's relevance and defining key terms.
- Articles: present selected research articles detailing each study's aims, methodologies, and limitations.
- Themes: discuss the key themes drawn from the reviewed literature, highlighting how they contribute to understanding the interplay between IR and PCOS.
- Conclusion: articulates a summary of the findings, emphasising how the research informs health promotion and disease prevention.

Through this structured approach, the report aims to distil complex scientific insights into actionable knowledge that can guide healthcare professionals in creating and implementing targeted interventions. These interventions aim not only to alleviate the metabolic and reproductive symptoms of PCOS but also to prevent the progression of related health complications.

Background

PCOS is a common hormone problem affecting roughly 1 in 15 women globally (Norman *et al.*, 2007). What Norman and his team's research shows is that PCOS leads to high male hormone levels, and it is correlated to issues with insulin, a sugar-regulating hormone. Women with PCOS can experience various health issues like irregular periods, difficulty getting pregnant, excessive skin hair growth, acne, weight gain and risks related to heart disease and diabetes (Bikman, 2020). The main signs of PCOS are hyperandrogenism, irregular or no ovulation, and many small cysts in the ovaries (Azziz *et al.*, 2006). Diagnosing PCOS can be complicated, and experts do not always agree on the best way to define it. The exact cause of PCOS is unclear, but it seems linked to genes and lifestyle factors (Teede *et al.*, 2010).

IR in the context of PCOS exacerbates symptoms and offers severe metabolic concerns. Insulin, a hormone the pancreas generates, contributes to blood sugar management (C. Ronald Kahn *et al.*, 1993). IR occurs when cells fail to respond adequately to insulin, resulting in a buildup of glucose in the bloodstream. IR not only increases the risk of Type 2 Diabetes in PCOS patients, but it also exacerbates the hormonal abnormalities that cause many of the disorder's symptoms (Diamanti-Kandarakis, 2007).

The link between IR and PCOS emphasises this domain's critical need for health promotion and illness prevention (World Health Organisation, 2023). When PCOS continues untreated or is poorly managed, reproductive health, a crucial part of overall health and well-being, is jeopardised. Given the high prevalence of PCOS and the potential for a cascade of health concerns, initiatives aimed at early detection, management, and awareness can have a substantial influence on public health (Fauser *et al.*, 2011).

Here are the key terms and concepts that help understand the topic:

1. PCOS: Polycystic Ovary Syndrome is a complex endocrine disorder associated with IR (Teede *et al.*, 2010).
2. Hyperandrogenism: A condition characterised by excessive levels of androgens (male sex hormones such as testosterone) in the female body and may be associated with conditions like PCOS (Azziz *et al.*, 2006).
3. IR: Insulin resistance is a diminished reaction to the hormone insulin. IR occurs when a cell ceases responding to insulin, which can be caused by various situations (Bikman, 2020).
4. Aldo-keto reductase family 1 member C3 (AKR1C3): An enzyme implicated in the overproduction of androgens within adipose tissue, potentially aggravating the symptoms and metabolic profile of women with PCOS (O'Reilly *et al.*, 2017).
5. Lipotoxicity: The pathological accumulation of lipids in non-adipose tissues leading to cellular dysfunction, often observed in the metabolic disturbances associated with PCOS (Sharma, 2002).
6. FTO Gene: A gene associated with fat mass and obesity, variations may influence body mass index and contribute to IR phenotype in women with PCOS (Frayling *et al.*, 2007).
7. Adipocytes: Adipose tissue-forming cells (Heilbronn & Campbell, 2008) that store fat and release hormones, playing a pivotal role in energy balance and influencing metabolic processes, including insulin sensitivity (Rosen & Spiegelman, 2006).
8. Fatty Acid Synthase (FASN): An enzyme involved in lipogenesis, found to be influenced by insulin and AKR1C3 activity in PCOS, linking hyperinsulinemia with lipid metabolism (Paulukinas and Penning, 2023).
9. Hyperinsulinemia: A condition with excess insulin circulating in the blood relative to the glucose level, often due to IR and a common feature in type 2 diabetes (Reaven, 1988).

10. **Androgens:** Steroid hormones that regulate the development and maintenance of male characteristics; in PCOS, increased androgen levels are a defining feature and contribute to the syndrome's clinical manifestations (Goodman *et al.*, 2015).
11. **Energy homeostasis:** The biological process by which the body regulates energy intake and expenditure to maintain energy balance and body weight (Schwartz *et al.*, 2000).
12. **Body Mass Index (BMI):** A statistical measure derived from the weight and height of an individual, commonly used to classify overweight and obesity, which is often higher in PCOS patients and affects insulin sensitivity (Ulijaszek, 2003).
13. **Health Promotion:** The process of enabling people to increase control over and improve their health. It represents a comprehensive social and political process that embraces actions directed at strengthening the skills and capabilities of individuals but also actions directed towards changing social, environmental, and economic conditions (World Health Organisation, 2023).
14. **Endocrine Disruptors:** Chemicals that can interfere with endocrine systems at specific doses may exacerbate PCOS symptoms and contribute to IR by affecting hormone regulation (Gore *et al.*, 2015).
15. **Ovarian Hyperstimulation:** A condition in PCOS where the ovaries are excessively stimulated, leading to multiple cyst formations and an imbalance of reproductive hormones (Fauser *et al.*, 2012).
16. **Chronic Inflammation:** PCOS has been associated with low-grade chronic inflammation, in association with IR and cardiovascular risk (González, 2012).
17. **Oxidative Stress:** An imbalance between antioxidants and reactive oxygen species in the body, oxidative stress may play a role in the pathophysiology of PCOS and IR (Li *et al.*, 2022).
18. **Glucose Tolerance Testing:** A method to assess insulin sensitivity and glucose metabolism, often used in diagnosing and managing IR (American Diabetes Association, 2020).

19. Biomarkers of PCOS: Various biomarkers, such as anti-Müllerian hormone (AMH) and Inhibin B, are investigated for their diagnostic potential in PCOS (Dewailly *et al.*, 2014).

Articles

These three articles are introduced, showing the sources, authors, aims, research methods, key terms and limitations.

Article 1:

Title: AKR1C3-Mediated Adipose Androgen Generation Drives Lipotoxicity in Women With Polycystic Ovary Syndrome.

Authors: Michael W. O'Reilly *et al.*

Published in: The Journal of Clinical Endocrinology and Metabolism, 2017, Vol.102 (9), p.3327-3339.

Aim: This study explores the role of AKR1C3-mediated androgen generation in adipose tissue and its contribution to lipotoxicity in women with PCOS.

Research Methods: Compared to ten body mass index-matched healthy controls, the researchers conducted a human in vivo metabolic phenotyping study -the analyses of biological fluids and tissues on live objects (Nicholson *et al.*, 2012), to examine the systemic and intraperitoneal effects of acute and chronic androgen exposure in 10 PCOS women, complemented by in vitro studies.

Key Concepts/Terms: AKR1C3 (Aldo-Keto Reductase Family 1 Member C3), Lipotoxicity, Androgens, PCOS.

Weaknesses/Limitations: Part of the study is limited by its in vitro nature, which may only partially replicate the complexity of metabolic pathways in living organisms. The sample size was relatively small, which may affect the generalisability of the findings.

Article 2:

Title: Large effects on body mass index and insulin resistance of fat mass and obesity-associated gene (FTO) variants in patients with polycystic ovary syndrome (PCOS).

Authors: Susanne Tan *et al.*

Published in: BMC Medical Genetics, 2010, Vol.11 (1), p.12-12, Article 12.

Aim: This research investigates the impact of FTO gene variants on BMI and IR in PCOS patients.

Research Methods: Researchers compared the effect of obesity risk alleles on BMI between PCOS patients and selected women in the same age group from a population study (Klüppelholz *et al.*, 2015). Researchers conducted an association study - that checks for dependencies in occurrences (Altman and Krzywinski, 2015), involving 386 individuals with PCOS who had single nucleotide polymorphisms within or adjacent to fat mass and various genes.

Key Concepts/Terms: FTO Gene, BMI (Body Mass Index), IR, PCOS.

Weaknesses/Limitations: The study's cross-sectional design does not allow for causal inferences. Additionally, the population was limited to a specific ethnic group, which may determine the applicability of the results to other populations.

Article 3:

Title: Insulin-Induced AKR1C3 Induces Fatty Acid Synthase in a Model of Human PCOS Adipocytes.

Authors: Ryan D. Paulukinas and Trevor M. Penning.

Published in: Endocrinology (Philadelphia), 2023, Vol.164 (5).

Aim: This study investigates how insulin induces the expression of AKR1C3 and fatty acid synthase in adipocytes, potentially contributing to the metabolic disturbances observed in PCOS.

Research Methods: Researchers utilised an experimental approach involving cultured human adipocyte models from women with PCOS. The cells were treated with insulin, and subsequent AKR1C3 and fatty acid synthase expression changes were measured.

Key Concepts/Terms: AKR1C3, Insulin, Fatty Acid Synthase (FASN), Adipocytes, PCOS.

Weaknesses/Limitations: The findings are based on a specific cell model and may not fully represent in vivo conditions. Extrapolating these results to the broader PCOS population may be premature without further clinical studies.

Themes

Theme 1

Androgen Excess and Adipose Tissue Dysfunction

O'Reilly *et al.* (2017) highlight the role of the AKR1C3 in promoting androgen excess within adipose tissue, leading to lipotoxicity, suggesting a novel intersection between hormone imbalance and metabolic dysfunctions in PCOS.

Implications for Health Promotion:

- Understanding this pathway opens possibilities for developing specific enzyme inhibitors as therapeutic agents, potentially reducing androgen excess and improving metabolic outcomes through non-pharmacological therapies focused on insulin sensitivity of the body cells in PCOS patients.

Theme 2

Genetic Influences on PCOS Phenotype

Tan *et al.* (2010) identify a significant association between variants of the FTO gene and increased BMI and IR in PCOS and point to a genetic susceptibility component that could exacerbate the PCOS phenotype.

Implications for Health Promotion:

- The results advocate for genetic screening in PCOS populations, which could lead to early identification of at-risk individuals and the provision of personalised lifestyle or pharmacological interventions to mitigate these risks.

Theme 3

Insulin Resistance and Lipid Metabolism

Paulukinas and Penning (2023) present evidence that insulin can induce the expression of fatty acid synthase via AKR1C3 in PCOS adipocytes, implicating IR in the dysregulation of lipid metabolism in PCOS.

Implications for Health Promotion:

- Therapeutic approaches that improve insulin sensitivity, such as diet, exercise, and potentially insulin-sensitising drugs, could directly influence the metabolic disturbances associated with PCOS, indicating a preventative strategy for the associated comorbidities.

Theme 4:

A Multifactorial Approach to PCOS

The collective insights from these studies reiterate that PCOS is not solely an endocrine disorder but also a metabolic one, with IR playing a central role. A recurring theme is the intricate relationship between androgen levels, genetic predisposition, and metabolic pathways.

Implications for Health Promotion:

- A multifactorial intervention strategy that combines lifestyle modification, targeted pharmacotherapy, and possibly genetic counselling holds promise for improving both reproductive and metabolic health in women with PCOS.
- Preventive measures that address diet and exercise can directly impact insulin sensitivity and thus serve as foundational components of any health promotion program targeting PCOS.

Conclusion

This academic report has provided a comprehensive analysis of the interrelationships between IR and PCOS, highlighting the significant impact on women's reproductive health. Central themes that advance our understanding of PCOS's pathophysiology and its broader health implications have been discerned by examining the findings from pivotal research articles.

The themes: 'Androgen Excess and Adipose Tissue Dysfunction', 'Genetic Influences on PCOS Phenotype', 'Insulin Resistance and Lipid Metabolism', and 'A Multifactorial Approach to PCOS', drawn from the research present a straightforward narrative: effective management of PCOS requires an understanding of its hormonal, genetic, and metabolic dimensions. By addressing IR, clinicians can influence the course of PCOS, potentially improving fertility outcomes and reducing the risk of long-term metabolic complications. The evidence points towards a personalised medicine approach, tailoring interventions based on the individual's genetic makeup, metabolic profile, and hormonal balance, which not only answers the pressing research question but also promises a more nuanced approach to health promotion and disease prevention in women with PCOS.

In conclusion, synthesising these research findings illuminates the complexity of PCOS and reinforces the need for an integrative approach to its management. By focusing on IR, genetic factors, and androgen excess, healthcare professionals can better guide health promotion and disease prevention strategies. This comprehensive approach has the potential to improve not only metabolic profiles but also reproductive health outcomes for women with PCOS, thereby enhancing their overall quality of life and well-being.

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