

METABOLIC DISORDERS IN POLYCYSTIC OVARY SYNDROME AND THEIR IMPACT ON FERTILITY

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Annotation : *This thesis examines the pathophysiological mechanisms underlying metabolic dysregulation in polycystic ovary syndrome and their consequent impairment of reproductive function. Through synthesis of contemporary clinical and molecular evidence, the study elucidates the interplay between hyperinsulinemia, androgen excess, and anovulation, offering a basis for integrated therapeutic strategies aimed at restoring metabolic homeostasis and fertility.*

Keywords: *polycystic ovary syndrome, hyperinsulinemia, insulin resistance, hyperandrogenism, anovulation, gonadotropin dysregulation, adipokines, ovarian folliculogenesis, metabolic syndrome, reproductive endocrinology.*

Today, polycystic ovary syndrome represents the most prevalent endocrine-metabolic disorder among women of reproductive age, affecting approximately 8-13% of this population worldwide, according to data published by the World Health Organization. The condition accounts for up to 80% of anovulatory infertility cases, constituting a major global reproductive health burden. Its pathogenesis is multifactorial, rooted in the complex interaction between insulin resistance, dyslipidemia, chronic low-grade inflammation, and disrupted hypothalamic-pituitary-ovarian axis signaling, all of which collectively compromise oocyte quality and endometrial receptivity.

The central metabolic aberration in polycystic ovary syndrome is insulin resistance, which manifests in approximately 65-70% of affected individuals regardless of body mass index. Compensatory hyperinsulinemia exerts direct stimulatory effects on ovarian theca cells, amplifying androgen biosynthesis through upregulation of cytochrome P450c17 enzymatic activity. The resulting hyperandrogenism suppresses hepatic synthesis of sex hormone-binding globulin, thereby elevating bioavailable testosterone and further disrupting follicular maturation. At the level of the hypothalamic-pituitary axis, elevated androgen concentrations accelerate gonadotropin-releasing hormone pulse frequency, producing a disproportionate elevation in luteinizing hormone relative to follicle-stimulating hormone. This hormonal imbalance arrests folliculogenesis at the antral stage, yielding the characteristic polycystic morphology and chronic anovulation that underlie infertility. Adipokines - including leptin, adiponectin, and resistin - mediate additional metabolic-reproductive crosstalk. Hyperleptinemia, commonly observed in patients with excess adiposity, impairs gonadotropin-induced steroidogenesis at the granulosa cell level, while reduced adiponectin concentrations further perpetuate insulin resistance and inflammatory signaling within the ovarian microenvironment. Concurrent dyslipidemia, characterized by elevated triglycerides and reduced high-density lipoprotein cholesterol, contributes to oxidative stress within the follicular fluid, diminishing oocyte developmental competence. From a therapeutic standpoint, insulin sensitizers - most notably metformin - reduce hyperinsulinemia and restore ovulatory cyclicity in a significant proportion of patients. Lifestyle modification, including structured caloric reduction and aerobic exercise, independently improves insulin sensitivity, lowers androgen levels, and increases the probability of spontaneous ovulation. In cases of pharmacological ovulation induction, letrozole has demonstrated superior clinical pregnancy rates compared with clomiphene citrate, attributed to its selective suppression of estrogen-mediated

negative feedback. Assisted reproductive technologies require individualized protocols accounting for the heightened risk of ovarian hyperstimulation syndrome in this population, necessitating careful gonadotropin dose titration and luteinizing hormone surge monitoring.

Metabolic dysfunction in polycystic ovary syndrome operates through interconnected endocrine pathways that fundamentally impair folliculogenesis and fertility. Future research should prioritize personalized therapeutic algorithms integrating metabolic, hormonal, and genetic profiling to optimize reproductive outcomes.

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