

INVESTIGATING GLP-1 FOR PCOS MANAGEMENT AND FERTILITY ENHANCEMENT

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Polycystic Ovary Syndrome (PCOS) is the most common endocrinopathy in women of reproductive age, with an astounding prevalence of 52% reported in Pakistan and a global prevalence of 6–8%.¹ PCOS is marked by skyrocketing androgen levels and irregular or absent ovulation. Patients suffering often experience the following co-occurring conditions: obesity, insulin resistance, impaired glucose metabolism, dyslipidemia, hypertension, metabolic syndrome, infertility, and an elevated risk of diabetes.^(2,3) About 50% of women with PCOS deal with obesity and 50–80% face insulin resistance.⁽²⁾ Obesity in particular exacerbates PCOS symptoms by impairing the hypothalamic-pituitary-ovarian (HPO) axis, which leads to poor oocyte quality and altered endometrial receptivity. Thus, adiposity significantly affects various PCOS phenotypes and is a prominent cause of infertility.^(1,3)

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have been a recent addition to the treatment options available for managing the metabolic symptoms of PCOS.⁽²⁾ Before starting GLP-1RA therapy, patients should get screened for any history of pancreatitis, diabetic retinopathy, or thyroid cancer.⁽²⁾ GLP-1RAs are drugs usually prescribed to type 2 diabetes mellitus (T2DM) patients to regulate their blood glucose levels by increasing insulin sensitivity.⁽³⁾ They can reduce hyperlipidemia and decrease glycated hemoglobin levels. Additionally, GLP-1RAs effectively minimize weight by slowing gastric emptying and achieving satiety by inhibiting neuropeptide Y and agouti-related peptides.⁽²⁾

Recently, there has been a rise in “ozempic babies” when women unexpectedly conceive after being on medications like semaglutide and other GLP-1RA drugs. A case report published in 2024 describes a 41-year-old obese female with T2DM and PCOS who continued using dulaglutide (a GLP-1 agonist) until 15 weeks gestation, delivering a healthy baby at 36 weeks. Considering all the factors that made it a high-risk pregnancy, there were no significant developmental defects observed from dulaglutide exposure.⁽⁴⁾ This report illustrates the potential for early pregnancy safety under GLP-1RAs, though more research is needed. GLP-1RAs have shown fetal defects in animal studies, and limited human research necessitates caution. Weight loss is crucial for enhancing fertility in PCOS; one study noted 90% ovulatory function restoration after a 6-month weight loss program.⁽⁴⁾ As GLP-1RAs gain popularity for weight loss in reproductive-age women, clearer guidelines are mandatory for safe pregnancy management.

In conclusion, although there isn't a direct relationship between

GLP-1RAs and fertility, they can significantly help manage the metabolic symptoms of PCOS and, in turn, improve fertility in women. This offers a new window of hope for those struggling to conceive. Procreation holds immense value in Pakistani culture, and women facing infertility often experience stigmatization (65% reported), threats of second marriages (72% reported), and inferiority (70.3% reported), according to a study done in Khyber Pakhtunkhwa.⁽⁵⁾ While implementing healthy lifestyle changes through diet and exercise should be the first line of action, GLP-1RAs provide a potential treatment option for those whose infertility due to PCOS and obesity remains unresolved. This approach could transform the lives of many women in Pakistan and globally, providing them with a much-needed solution to fulfill their desire for parenthood.

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