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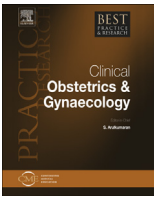

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Polycystic ovary syndrome: Endometrial markers

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Women with polycystic ovarian syndrome (PCOS) present with several endometrial abnormalities possibly explaining some of the adverse endometrium-related outcomes in these women. PCOS and an increased miscarriage rate have been suggested to coincide, but the results are conflicting. Recent studies have also shown increased risks of pregnancy-induced hypertension, preeclampsia, and premature delivery that may be related to altered decidualization/placentation in affected women. In the long run, PCOS per se is associated with the occurrence of endometrial cancer (EC), with obesity aggravating the risk.

Most investigated markers of the endometrial abnormalities in women with PCOS are related to steroid hormone action (ERs (estrogen receptors), PRs (progesterone receptors), ARs (androgen receptors), and steroid receptor coactivators), endometrial receptivity/decidualization (*HOXA10,* αvβ3 integrin, and IGFBP-1 (insulin-like growth factor-binding protein 1)), glucose metabolism (IRs (insulin receptors), glucose transporters, IGFs) and inflammation/immune cell migration (IL6 (interleukin 6), CCL2 (C–C motif ligand), and uNK (uterine natural killer) cells). Despite several endometrial abnormalities in women with PCOS, the clinical relevance of these findings still awaits future clarification; to date, no common screening protocols/recommendations for women with PCOS have been established.

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Endometrial dysfunction in women with pcos

Endometrial pathologies related to reproductive functions

Q1 Several studies suggest an abnormal endometrial phenotype and function in women with polycystic ovary syndrome (PCOS) [1]. In the past years, several investigators reported an increased risk of early miscarriage in women with PCOS as one of the first clinical findings [2–5]; however, not all studies agree [6]. Some investigators report PCOS per se as an independent risk factor of miscarriage [7]; however, obesity and assisted reproductive technologies (ARTs), and recently hyperhomocysteinemia, have been shown to be associated with this risk in these women [4,8,9]. While different PCOS phenotype-specific analyses are limited, oligo-amenorrhea has been suggested as one of the factors increasing the rate of miscarriage in affected women, whereas polycystic ovaries do not seem to add to the risk [7,9].

Adverse pregnancy outcomes have also been associated with PCOS. Affected women have been shown to present with a three- to fourfold increased risk of pregnancy-induced hypertension and preeclampsia and a twofold higher chance of premature delivery [10]. Given this, it is likely that severe PCOS and its metabolic phenotype (amenorrhea, hyperandrogenism, obesity, diabetes, and hypertension) can affect the periconceptional endometrial milieu, leading to impaired placentation and promoting pregnancy complications that are also suggested to have an effect on the offspring [11] (Fig. 1). In fact, some adverse outcomes may be derived from abnormal trophoblast invasion and placentation in cases of PCOS, and surprisingly altered placental morphology has been reported even in spontaneous, uncomplicated PCOS pregnancies [12–14]. Regarding the ART outcomes, a recent study showed an association between the increased number of oocytes retrieved in cases of IVF (in vitro fertilization; a common finding in women with PCOS undergoing gonadotropin stimulation) and preterm birth and low birth weight; this again suggests that abnormal placentation and an altered endometrial milieu may contribute to these events [15]. Future elective embryo cryopreservation studies may partly elucidate the role of endometrial stress related to the IVF treatments and the role of endometrial health in cases of PCOS [16].

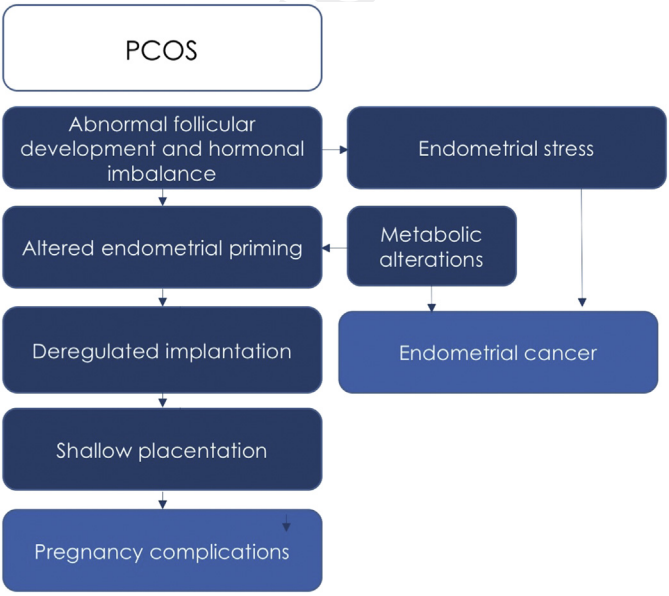

Fig. 1. Endometrium-related pathogenesis in women with PCOS, resulting in adverse pregnancy outcomes and endometrial cancer.

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