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Estrogenized mouse model of polycystic ovary highlights mitochondrial pathway of apoptosis

Gayatri Shinde[1], Sushma Khavale[1], Roshan Dadachanji[1], Serena D'Souza[2], Tarala Nandedkar[3] & Srabani Mukherjee[1]*

[1]Department of Molecular Endocrinology, ICMR-National Institute for Research in Reproductive Health, JM Street, Parel, Mumbai-400 012, Maharashtra, India

[2]Department of Virology, ICMR-National AIDS Research Institute, 73, 'G'-Block MIDC Bhosari, Pune-411 026, Maharashtra, India

[3]Haffkine Institute for Training, Research and Testing, Acharya Donde Marg, Parel, Mumbai-400 012, Maharashtra, India

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Polycystic ovary syndrome, which is a major cause of anovulatory infertility in women, featured by an ovarian morphology that reflects arrested follicular growth and accumulation of cystic follicles. Alteration of apoptotic process may promote development and persistence of follicular cysts, which has not been explored in details. Female animals exposed to estrogenic compounds at specific growth stages show altered pubertal maturation, ovulatory dysfunction, accumulation of follicular cysts and infertility. Here, we developed a mouse model of cystic ovary by neonatal estrogenization and investigated apoptotic changes underlying cystogenesis across various time points. We compared pro- and anti-apoptotic markers along with ovarian morphology between control and estradiol treated mice using several techniques including flow cytometry, immunohistochemistry and electron microscopy. Treated mice presented with cystic follicles with degenerated oocyte and reduced granulosa cell layer, anovulation, along with persistent estrus cycle and infertility. Increased apoptosis was demonstrated in cystic follicles with significantly increased expression of JC-1, Bid, caspase-9 and caspase-3. Thus, our findings highlight the involvement of mitochondrial pathway of apoptosis in development of polycystic ovary in response to neonatal exposure to estrogen. This model may serve to delineate the effect of environmental estrogen exposure to altered ovarian physiology which is frequently observed in PCOS women.

Keywords: Cystic follicles, Estrogen, Infertility, Neonatal estrogenization, Polycystic ovary syndrome (PCOS)