Cigarette smoking (CS) has some detrimental effects that occur via oxidative stress (OS). The aim of this work was to demonstrate the pathological and immunohistochemical effects of CS and the protective effects of a strong antioxidant alpha lipoic acid (ALA) on CS-induced genital system changes in a rat model. Twenty-eight female rats were randomly allocated to three groups as control, CS-exposed, and CS-exposed and ALA-treated. Reproductive tract organs were collected for biochemical and pathological examinations. In the CS group, OS markers increased in the tissues of both the ovary and fallopian tubes. Decreased follicle numbers in the ovary, marked ciliated loss in the fallopian tubes, and pathologic changes in the uterus were observed in the CS group. Positive calcitonin gene-related peptide (CGRP), caspase 3?, hypoxia-inducible factor 1? (HIF-1?), tumor necrosis factor-? (TNF-?) immunoreactions were observed in uterine tissues and HIF-1? immunoreactions in tubal and uterine epithelial cells of the CS group. ALA reversed all these findings effectively. CS has negative effects on the female reproductive system via HIF-1? in tuba uterina and HIF-1?, HIF-2?, TNF-?, caspase 3, and CGRP in the uterus, and ALA could protect against the negative effects of CS on the female reproductive system.