Oocyte endowment dwindles away during pre-pubertal and adult life until menopause occurs and apoptosis is identified as a central mechanism responsible for oocytes elimination. A few recent reports suggested that uncontrolled inflammation may adversely affect ovarian reserve. We tested the possible role of the pro-inflammatory cytokine Interleukin (IL)-1 in the age related exhaustion of ovarian reserve using IL-1α and IL-1β knock-out (KO) mice. IL-1α-KO mice showed a substantially higher pregnancy rate and litter size compared to WT at advanced age. The number of the secondary and antral follicles was significantly higher in 2.5 month old IL-1α-KO compared to WT ovaries. Serum anti-mullerian hormone (AMH), a putative marker of ovarian reserve, was markedly higher in IL-1α-KO mice from 2.5 months onwards, along with a greater ovarian response to gonadotropins. IL-1β-KO mice displayed a comparable but more subtle prolongation of ovarian life-span compared to IL-1α-KO mice. The protein and mRNA of both IL-1α and IL-1β were localized within developing follicles (oocytes and granulosa cells) and their ovarian mRNA levels increased with age. Molecular analysis revealed a decreased apoptotic signaling (higher BCL-2 and lower Bax protein levels) along with a marked attenuation in the expression of genes coding for the pro-inflammatory cytokines IL-1β, IL-6 and TNF-α in ovaries of IL-1α-KO compared to WT mice. Taken together, IL-1 emerges as an important participant in the age related exhaustion of ovarian reserve in mice possibly by enhancing the expression of inflammatory genes and promoting apoptotic pathways.