Methamphetamine is a recreational drug that can be taken ingestion orally, injected,smoked or snorted. Methamphetamine abuse may lead to male infertility. The purpose of this study was to evaluate the long term effects of methamphetamine abuse on the sex reprogramming of human post-mortem testis. Testes were collected from the autopsies of methamphetamine users (n = 10) and healthy males (reference group) (n = 10). They were then taken for stereological studies and RNA extraction to evaluate the expressions of PCNA, DMRT1, SOX8, c-Kit, TNF-α, IL6 and FOXL2 genes. In addition, Reactive Oxygen Species (ROS) level and Glutathione Disulfide (GSH) were assessed. Autopsied testicular samples of methamphetamine revealed a significant reduction in stereological parameters and histopathological findings, suggesting methamphetamine as a practical approach to prevention strategies in reproductive medicine that can disrupt spermatogenesis. Moreover, the results indicated the expressions of the genes involved in testis function and male-to-female genetic reprogramming (PCNA, DMRT1, SOX8, c-Kit, TNF-α, IL6 and FOXL2) (16) as well as in increasing inflammation (TNF-α and IL-6). The results also showed a high level of ROS and a decrease in GSH activity. The results of SOX9 immunohistochemistry indicated a significant decrease in the expression of SOX9 as well as in the number of Sertoli cells in the methamphetamine group. Overall, the results suggested that methamphetamine abuse caused spermatogenesis disruption and genetic reprogramming, probably through .oxidative stress and changes in the expression of sex-determining genes