

### **Abstract**

Infertility is on the rise worldwide and male factor contribution to infertility is ~30%. Reactive oxygen species (ROS) may have detrimental or beneficial effect on the male reproductive system. Oxidative stress (OS) plays a critical role in male infertility. While increased ROS generation reduces semen quality by damaging the sperm membrane and genetic material, optimum ROS is needed for sperm physiological processes like capacitation, acrosome reaction and fertilization. In the first part of the study, the effect of excessive and inadequate generation of ROS on semen quality and sperm fertilizing ability is studied. Since the intracytoplasmic sperm injection (ICSI) technique bypasses the normal sperm selection mechanism, thereby increasing the risk of transmitting OS induced damaged DNA, the safety of this technique is still a matter of concern. Effect of OS on sperm plasma membrane integrity and DNA fragmentation in ICSI is investigated. Excessive generation of ROS was found to have a significantly adverse effect on semen quality, fertilization and pregnancy outcome when ROS > upper control limit. Upper cut-off level of ROS beyond which fertilization rate is adversely affected was found to be  $\sim 75000-1 \times 10^6$  cpm/10 million cells. However, follow-up on ICSI off-springs up to three years did not reveal any birth defects. A group of male partners of unexplained infertile couples with repeated intra-uterine insemination failure were observed to be associated with significantly low ROS level when compared to proven fertile men. Though no correlation between low ROS level and capacitation was observed, it was interesting to find that 47% of these cases had impaired tyrosine phosphorylation, which is an early event in the capacitation process. The present findings suggest that ICSI appears to be the treatment of choice in unexplained couples with defective capacitation. Though it is believed that antioxidant administration may reduce semen ROS generation and also improve semen quality, controversies still exist. In the last part of the study, the effect of oral antioxidant supplementation on semen quality is explored. A significant increase in sperm count and decrease in ROS levels were observed after three months of antioxidant intake. It is, therefore, suggested that in cases with male factor defect, antioxidant therapy prior to ICSI treatment may considerably increase the chances of success rate.

**Key words:** Oxidative stress, Intracytoplasmic Sperm Injection (ICSI), Unexplained infertility, Capacitation, Antioxidant supplementation