Conclusions

1. In a preliminary study, employing alkaline comet assay, it has been demonstrated that DNA damage is higher in infertile men in comparison to fertile controls (specifically those with idiopathic infertility and oligozoospermia), which provided a rationale for further continuation of the work proposed in the thesis.

2. The average incidence of sperm DNA damage in patients with idiopathic male infertility is <10% whereas patients with oligospermia, severe oligospermia, necro spermia and multiple sperm abnormalities (oligoasthenoteratospermia) had significantly higher level of DNA damaged sperm suggesting poor semen quality is associated with increased level of DNA damaged sperm.

3. The association between men’s age and sperm DNA damage observed in this study suggests paternal sperm integrity declines with ageing. Since this issue is contradictory, it needs to be confirmed by multi-centric studies using large number of study subjects.

4. Sperm DNA damage was specifically increased in subjects with varicocele and history of alcohol consumption. However, no significant association was observed between sperm DNA damage, duration of infertility, pregnancy loss in partner, occupational factors and smoking.

5. Although preliminary studies revealed a possible association between sperm head abnormality and increased DNA damage, subsequent studies employing alkaline comet assay failed to reveal any significant association.

6. Viable sperm selected by hypoosmotic swelling test have been found to possess superior DNA integrity, suggesting that it may be used for non-destructive, selective identification of viable spermatozoa with minimal DNA fragmentation for use in ART.
7. Currently used sperm selection methods have been found to effectively eliminate sperm with DNA damage, as a consequence of which the risk of using a genetically incompetent sperm for medically assisted conception and assisted reproduction seems to be low.

8. Sperm DNA damage does not appear to influence either the establishment or maintenance of a viable pregnancy in medically assisted conception (IUI) and assisted reproduction. Although DNA damage in the sperm is expected to induce defective fertilization and variety of damage response in the embryos, this study did not show any significant differences with respect to fertilization rate, embryonic development rate, embryonic fragmentation and the implantation potential in ART.

9. Moreover, neither the TUNEL assay which measures DNA strand breaks nor the sperm chromatin structure assay (SCSA), which measures susceptibility to DNA denaturation in situ, was predictive adverse reproductive outcome when IUI or ART is employed. Overall, although the results from this study demonstrated the association between standard semen parameters and sperm DNA damage, no association was found between sperm DNA damage and reproductive outcome in the partners.

10. Using $^1$H-NMR spectroscopy, biochemical differences between different forms of male infertility, specifically idiopathic infertility has been identified. The results suggest that future attempts to achieve a complete assignment of the $^1$H NMR metabolic profile for seminal fluid may enhance the information obtainable from metabolomic studies and aid as a valuable tool in the diagnosis and management of infertility.