



**The Effect of Paternal Obesity on Sperm
Function, Embryo Development and
Subsequent Pregnancy Outcomes**

Hassan Waleed Bakos

B.Hlth.Sc.(Hons.)

Discipline of Obstetrics and Gynaecology

School of Paediatrics and Reproductive Health

Faculty of Health Sciences

The University of Adelaide

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Thesis abstract

Obesity and its health consequences are an increasing health burden for Australian society, with more than seven million adults in Australia being overweight or obese. According to the Burden of Disease and Injury in Australia (BoD) study, high body mass was responsible for 7.5% of the total burden of disease and injury and is increasing. It is now clear that maternal obesity reduces fertility, in part through actions on the egg, which affect the health of the resultant pregnancy. However, the potential role of male obesity in infertility has been essentially ignored. This is surprising, as the male gamete contributes half of the genetic material of the embryo. Furthermore, sperm function constitutes the single most common cause of infertility. Therefore, factors influencing the health of the sperm and the underlying mechanisms behind any pathology are paramount.

The overall aim of this thesis was to determine the relationship between paternal obesity and male fertility. A novel and unique animal model was developed to elucidate the effects of paternal obesity on embryo development and pregnancy. Results showed that paternal obesity has negative effects on both sperm quality as well as embryo development and quality.

To confirm the results seen in the mouse, the pregnancy and live birth outcomes of a large cohort of patients undergoing assisted reproductive technology were assessed in relation to male obesity. Confirming the results observed in the mouse, it was clearly demonstrated that both sperm function parameters as well as embryo development were significantly reduced where the male partner is obese. This observation was evident after controlling for important factors such as maternal and paternal age as well as maternal body mass index (BMI). Furthermore, clinical pregnancy rates were reduced, miscarriage rates increased and live birth rates were reduced.

Moreover, analysis revealed that as paternal BMI increased, both seminal plasma glucose as well as insulin levels also increased, implicating the role of glucose, in particular, as detrimental to sperm function.

To further elucidate the metabolic markers involved, additional in-vitro studies were conducted whereby factors such as elevated glucose were shown to negatively affect sperm quality in vitro with elevated reactive oxygen species levels and DNA damage observed. These results are consistent with the effects seen on obese men and mice.

In summary, the current studies have shed some light on some longstanding questions regarding the effects of paternal obesity on fertility. Additional questions have been raised as to further understanding the mechanisms behind these effects (and their potential reversibility). This thesis has shed some much-needed light on a major knowledge gap in men's health and will undoubtedly stimulate further interest in this very important area of applied science and medicine.

Declaration

This work contains no material that has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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Hassan W. Bakos

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Abstracts arising from this thesis

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Other abstracts

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