

**INFERTILITY TREATMENT OUTCOME EVALUATION
IN INFERTILE OBESE PATIENTS UNDERGOING
INTRACYTOPLASMIC SPERM INJECTION**

Thesis

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Abstract

The aim of this study to observe the impact of obesity on the outcome of IVF and ICSI cycles and to compare the outcome of IVF or ICSI treatments in obese patients to that in morbidly obese patients. A total of 120 patients undergoing ICSI cycles were categorized on the basis of body mass index: (group A 30-34.9 group B ≥ 35 & and group C < 30). No statistically significant difference among the three groups of patients as regard all the parameters of the outcome including dose and duration of drug used for stimulation, number of oocytes retrieved ,number of embryos obtained and finally the implantation rate.

Keywords: Assisted reproduction treatment, Body mass index, IVF, Obesity, Intracytoplasmic sperm injection.

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LIST OF ABBREVIATIONS

AFC	Antral Follicle Count
ET	Embryo Transfer
FSH	Follicle Stimulating Hormone
GLUT4	Glucose Transporter 4
GNRH	Gonadotropin Releasing Hormone
HPO	Hypothalamo- Pituitary Ovarian
IGF	Insulin like Growth Factor
IGFBP1	Insulin like Growth Factor Binding Protein 1
IL6	Interleukin-6
IVF	In Vitro Fertilization
LH	Luteinizing Hormone
M2	Metaphase 2 oocyte
NICE	National Institute for Clinical Excellence
OE2	Estradiol
PAI1	Plasminogen Activator Inhibitor type-1
PCOS	PolyCystic Ovary Syndrome
PRL	Prolactin
TNF	Tumour Necrosis Factor
ROC	Receiver Operating Characteristic

RT-PCR	R ecombinant P olymerase C hain R eaction
SHBG	S ex H ormone B inding G lobulin
SC	S ubcutaneous
WHR	W aist - H ip R atio
WMD	W eighted M ean D ifference



INTRODUCTION

Introduction

Rising obesity rates present a global public health challenge. The World Health Organization (WHO) issued the fact that approximately 1.6 billion adults worldwide were overweight (BMI 25-30 kg/m²) and at least 400 million were obese (BMI >30 kg/m²) in 2005. These figures are expected to rise to 2.3 billion and 700 million, respectively, by 2015 (Facts about overweight and obesity (2010)). In the West, 56% of women in England (*Health Survey for England, 2007*) and 61% women in the United States are believed to be either overweight or obese (*Ogden et al. 2004*). The prevalence of obesity is relatively low in Asian countries with 4% of Chinese and 0.5% of Indian women noted to be obese (*Prentice et al. 2006*). Nevertheless, in the last 20 years, the obesity rates have tripled in the developing world and 10% of all children across the world are overweight or obese (*Hossain et al. 2007*).

The worldwide trend of rising obesity rates, particularly in Western countries, is attributed to a combination of reduced exercise, changing dietary composition and increased energy intake. In USA and many European countries more than half of the adult population is overweight and up to 30% are clinically obese. In Australia 52% of women are overweight or obese (*International Obesity Task Force and European Association for the Study of Obesity, 2002 & Norman et al. 2004*).

Furthermore, many ethnic groups who either migrate to Western societies or adopt a Western lifestyle are prone to obesity in their changed environment (*Norman et al. 2004*). In fact, in 2000, obesity affected 300 million adults throughout the world (*Hall and Neubert, 2005*).

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The formula that is universally used in medicine for showing pathology in body mass of the human body is the body mass index (BMI) (*Eknoyan Garabed. 2008*).

Body mass index is defined as the quotient of the weight of the individual expressed in kilograms and height in meters squared kg / m^2 . The initiation and maintenance of reproductive functions are related to an optimal body weight in women. Underweight (BMI under 19 kg/m^2), as well as overweight (BMI over 25 kg/m^2) and obesity (BMI over 30 kg/m^2) are associated with an increased risk of certain disorders. The most common are: menstrual cycle disorders, the occurrence of an anovulatory infertility and a pathological condition during pregnancy (*Sharpe et al. 2004, American College of Obstetricians and Gynecologists, 2005*).

This pathology is the result of multiple endocrine and metabolic disorders that disrupt the balance through several mechanisms, directly and indirectly. It has been proven that fat tissue affects the secretion of sex hormones and their bio-availability. Indirectly, obesity exerts its effect via leptin, insulin and adipokines (*Poretsky et al. 1999, Moschos et al. 2002, Pasquali et al. 2003, Fedorcsak et al. 2004, Pasquali et al. 2006 & Tang et al. 2006*).

Obesity has been related to increased morbidity and mortality rates, the former in terms of pathologies such as cardiovascular and cerebrovascular disease, type II diabetes, sleep apnea, gastrointestinal diseases, arthritis and cancer (*Norman and Clark, 1998, Calle et al. 1999, 2003 & van Swieten et al. 2005*). In the field of gynecology and reproduction, obesity is associated with menstrual disorders, hirsutism, infertility, miscarriage and obstetric complications (*Norman et al. 2004*

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& Pasquali and Gambineri, 2004). These disturbances have been related to obesity itself or/and to polycystic ovarian syndrome (PCOS), frequently associated with an increased body mass index (BMI). In fact, over one-third to one-half of PCOS subjects are overweight or obese (**Balen et al. 1995 & Gambineri et al. 2002).**

Obesity is known to impair human reproduction through different mechanisms such as insulin resistance, hyperandrogenism and elevated leptin levels. Weight management and dietary intervention can reverse this situation and improve reproductive function (**Pasquali et al. 2003, Linne, 2004, Norman et al. 2004 & Pasquali and Gambineri, 2004).**

Clinical observation on the effect of body weight during IVF is interesting and controversial. Overall, most studies have shown that overweight and obesity have a negative impact on the success of IVF (**Loveland et al. 2000, Wang et al., 2000, Nichols et al. 2003, Ferlitsch et al. 2004 & Lintsen et al. 2005).** but there are studies that have not found negative impact (**Lashen et al. 1999, Wittemer et al. 2000, Frattarelli et al. 2004, Spandorfer et al. 2004, van Swieten et al. 2005 & Dokras et al. 2006).**

Obesity has been reported to affect Controlled Ovarian Hyperstimulation (COH) in women undergoing treatment. Reported effects include prolonged COH, increased dose requirement of gonadotrophin, increased incidence of follicular asynchrony and increasing cancelled cycles (**Mulders et al. 2003, van Swieten et al, 2005, Balen et al. 2006, Maheshwari et al. 2007 & Esinler et al. 2008).** All this leads to a smaller percentage of clinical pregnancies and a lower percentage of births (**Loveland et al. 2000, Wang et al.,2000, Nichols et al. 2003,Ferlitsch et al. 2004,Fedorcsak et al. 2004 & Lintsen et al.**

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2005). Additionally, obese women who conceive following IVF have been found to be at increased risk of an early pregnancy loss (*Wang et al. 2000 & Fedorcsak et al. 2004*).

In our study we are trying to find out if obesity as a sole factor can affect the outcome of IVF or ICSI cycles and leads to unfavorable results or not.

AIM OF THE WORK

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To compare the outcome of IVF or ICSI treatments in obese patients (BMI = 30–34.9 kg/m²) to that in morbidly obese patients (BMI $\geq$ 35 kg/m²).