ROLE OF MATERNAL EXPOSURE TO HEAVY METALS POLLUTION ON THE SUCCESS RATE OF IN-VITRO FERTILIZATION

Thesis

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By

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List of Abbreviations

AA	*Ascorbic acid*
AMH	*Anti-mullerian hormone*
ART	*Assisted reproductive technologies*
ATSDR	*The agency for toxic substances and disease registry*
BAI	*British anti lewisite*
BMP-15	*Bone morphogenic protein-15*
BTB	*Blood-testis barrier*
CD	*Cadmium*
CDC	*Centers for disease control and prevention*
CGH	*Comparative genomic hybridization*
CI	*Confidence interval*
COH	*Controlled ovarian hyperstimulation*
CU	*Copper*
CVS	*Chorionic villus sampling*
DMSA	*di-mercaptoproan-sulphonic acid*
E_2	*Estradiol*
EPA	*Environmental protection agency*
ET	*Embryo transfer*
FF	*Follicular fluid*
FISH	*Fluorescence in situ hybridization*
FP	*Fragmentation pattern*
FSH	*Follicle stimulating hormone*
GH	*Growth hormone*
GIFT	*Gamete intrafallopian transfer*
GnRH	*Gonadotropin releasing hormone*
HCG	*Human chorionic gonadotropin*
HLA	*Human leukocyte antigen*
ICSI	*Intracytoplasmic sperm injection*
IVF	*In-vitro-fertilization*
LH	*Luteinzing hormone*
LH	*Luteinizing hormone*
LPS	*Luteal phase support*
MII	*Metaphase II*

MS	*Mass spectrometry*
MT	*Metallothionein*
NAG	*N-acetyl-beta-gluconamidase*
OCC	*Oocyte-cumulus complexes*
OHSS	*Ovarian hyperstimulation syndrome*
OPU	*Oocyte pick up*
OR	*Odds ratio*
P	*Progesterone*
PB	*Lead*
PCO	*Polycystic ovary*
PCR	*Polymerase chain reaction*
PGD	*Preimplantation genetic diagnosis*
PGS	*Preimplantation genetic screening*
PRL	*Prolactin*
PTWI	*Provisional tolerated weekly intake*
RH	*Rhesus factor*
ROS	*Reactive oxygen species*
SC	*Subcutaneously*
sGE	*Superficial glandular epithelia*
SOD	*Super oxide dismutase*
TAC	*Total antioxidant capacity*
TET	*Tubal embryo transfer*
TNF	*Tumor necrosis factor*
UPLC	*Ultra performance liquid chromatography*
WHO	*World Health Organization*
ZIFT	*Zygote intrafallopian transfer*
Zn	*Zinc*

ABSTRACT

The study investigated the effect of lead, cadmium and mercury exposure on pregnancy and fertilization rate outcome among 200 women one hundred of them taken as study group and the others taken as control group, the study group was suffering form primary or secondary infertility and who sought in vitro fertilization (IVF) treatment.

The concentrations of lead, cadmium and mercury were measured in blood, results revealed that there is no statistically significant difference between study and control groups as regard, weight, height, educational level and economic level also use of contraception but thee is significiant difference between study and central groups as regard distribution of cases according to their residence.

The positive pregnancy rate among study group was 33% with signficiant increase in serum lead, cadmium and mercury levels in failed cases (negative pregnancy cases) in comparison to their values in positive cases which points to the necessity for further investigations.

INTRODUCTION

Infertility is common, approximately 10% of couples have difficulty conceiving a child. In young, healthy couples, the probability of conception in one reproductive cycle is typically 20 to 25%, and in 1 year it is approximately 90% ***(Gnoth et al., 2003).***

An evaluation is commonly recommended after 1 year of unprotected intercourse without conception, the standard clinical definition of infertility. Many infertility specialists are surprised by the number of otherwise highly educated older couples with unrealistic expectations of fertility. The negative effect of a woman's age on fertility cannot be overemphasized. As women age, fertility declines and the rate of miscarriages increases. In addition, the rate of pregnancy after treatment for infertility drops more rapidly in women who are over the age of 35 years than in younger women. Thus, some clinicians argue that an infertility evaluation should begin after six cycles of unprotected intercourse in women older than 35 years ***(Gnoth et al., 2005).***

Several societal factors may contribute to infertility related to aging in women. In the United States, there have been increases over time in the mean maternal age at first birth (25.1 years in 2002 vs. 21.4 years in 1968) and in the

mean age of women delivering a child (27.3 years in 2002 vs. 24.9 years in 1968) ***(Hamilton and Ventura, 2002).***

This trend toward delayed childbearing in part reflects an increasing emphasis on career and educational goals as well as a later mean age at first marriage. In addition, the increased availability of effective methods of birth control makes it more likely that earlier unplanned pregnancies will be avoided ***(Schoen and Canudas-Romo, 2005)***

Regardless of the cause of infertility, the treatment that leads to the highest pregnancy rate per cycle is in vitro fertilization (IVF). Since its inception in 1978 ***(Steptoe and Edwards, 1978),*** there has been a remarkable increase in the numbers of IVF cycles worldwide. Approximately 1 in 50 births in Sweden, 1 in 60 births in Australia, and 1 in 80 to 100 births in the United States now result from IVF. In 2003, more than 100,000 IVF cycles were reported from 399 clinics in the United States, resulting in the birth of more than 48,000 babies ***(Van Voorhis, 2007).***

Heavy metals exposure has been identified as a factor affecting human fertility ***(Sharara et al., 1998).***

They may induce hormonal disorders, preventing ovulation and pregnancies ***(Choi et al., 2004)*** as well as abnormalities in sperm production ***(Sinawat, 2000).***

Maternal blood lead levels of approximately 10 mg/dL have been linked to increased risks of pregnancy hypertension, spontaneous abortion and reduced offspring neurobehavioral development ***(Bellinger, 2005).***

Cadmium is highly toxic, and one of the most important environmental pollutants in industrialized countries. It accumulates in the human body during lifetime and can induce renal dysfunction ***(Bernard, 2004).***

Mlynarcikova et al. (2005) reported that harmful effects of cigarette smoke components (cadmium, nicotine and cotinine) can disturb the intrafollicular process, leading to infertility.

Mercury and its compounds have a wide spectrum of toxicities, depending on the chemical forms and modes of exposure ***(Satoh, 2003).***

There have been numerous studies on the effects of mercury on the immune system, renal system, cardiovascular, reproductive system and the central nervous system **(Zahir et al., 2005).**

Mercury resulted in reproductive problems, such as spontaneous abortion, stillbirths, congenital malformations, infertility, disturbances in the menstrual cycle, inhibition of the ovulation and behaviourial effects of the offspring ***(Yoshida, 2003).***

AIM OF THE STUDY

The aim of this study is to:

- Evaluate the role of maternal exposure to heavy metal on the outcome of in-vitro fertilization.
- Find a standard method to select women to undergo in-vitro fertilization.

ASSISTED REPRODUCTION

Since the advent of in vitro fertilization (IVF) and the successful birth of Louise Brown on July 25, 1978, more than 3 million children have been born worldwide through assistive reproductive technologies (ART) ***(Steptoe and Edwards, 1978).***

In 2005, the 422 fertility clinics in the United States reported performing 134,260 ART cycles resulting in 38,910 live births of 52,041 children ***(CDC, 2005).***

Approximately, 1% of all births and 18% of all multiple births in the United States are the result of assisted reproductive technologies ***(Hamilton et al., 2006).***

Assisted reproductive technology includes all treatments that involve manipulation of both eggs and sperm outside of the body. Most commonly, it refers to in vitro fertilization, although other forms of ART used include gamete intrafallopian transfer (GIFT), zygote intrafallopian transfer (ZIFT), tubal embryo transfer (TET), donor oocyte, and gestational carriers. Other commonly used strategies to treat infertility, including ovulation induction and intrauterine inseminations, are not considered forms of ART. Ovulation induction stimulates multifollicular development with the use of oral or injectable medication without retrieving oocytes.