Effect of Vitamin D Status on Clinical Pregnancy Rates Following intra cytoplasmic sperm injection

Thesis

Submitted for Partial Fulfillment of the Master Degree in Obstetrics & Gynecology

By

Shaymaa Sayed Ahmed Alshabrawy
M.B., B.Ch- Cairo University, 2010
Resident of Obstetrics and Gynecology
Almataria Teaching Hospital

Under Supervision of

Prof. Adel Shafik Salah El-Din
Assistant Professor of Obstetrics and Gynecology
Faculty of Medicine - Ain Shams University

Dr. Bassem Aly Islam
Lecturer in Obstetrics and Gynecology
Faculty of Medicine - Ain Shams University

Dr. Mohammed Mahmoud Samy
Lecturer in Obstetrics and Gynecology
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
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Abstract

Introduction: Infertility, in general is defined as inability of a couple to achieve a pregnancy after a year of unprotected attempt to conceive a child. Global data suggests that almost 15% of couples, who wish to have a child, suffer from infertility; for which males and females are found to be equal contributors. Infertility can be broadly categorized into explained, reasons for which vary from failure of conception due to reproductive health issues of a male or female partner.

Aims: This study aims to investigate the association between vitamin D status and clinical pregnancy rates in women undergoing ICSI.

Methodology: Study setting: Ain Shams University Maternity Hospital. Study duration: March 2016 - November 2016 Number of patients: Included 240 patients. Study Design: A prospective Cohort study. The study was registered on ClinicalTrials.gov Clinical Trials.gov identifier: NCT02987478

Results: The current study was conducted at Ain Shams University Maternity Hospital during the period between January 2016 and November 2016. A total of 240 women planned to undergo IVF/ICSI for unexplained infertility were included.

Conclusion: The current study showed a significant association between reduced serum vitamin D and lower clinical pregnancy rate after IVF/ICSI in women with unexplained infertility.

Recommendations: Clinical trials are needed to address whether vitamin D and calcium supplementation would improve clinical pregnancy outcome following IVF/ICSI in such group of women.

Keywords: Vitamin D, Clinical Pregnancy Rates, Intra cytoplasmic, Sperm injection

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Contents

List of Abbreviations

AFC : Antral follicular count

AMH : Anti-Mullerian hormone

ART : Assisted reproductive technology

BMI : Body mass index

CC : Clomiphene citrate

FSH : Follicle stimulating hormone

FSH : Follicle stimulating hormone

GnRH-a : Gonadotropin releasing hormone analogue

GCs : Granulose cells

hCG : Human chorionic gonadotropin

hMG : Human Menopausal Gonadotropin

ICSI : Intracytoplasmatic Sperm Injection

IU : International units

IVF : In-vitro fertilization

LH : Luteinising hormone

OC : Oral contraceptive

OHSS : Ovarian hyperstimulation syndrome

PCOS : Polycystic ovary syndrome

RCT : Randomized controlled trial

RDA : Recommended Daily Allowance

SHBG : Sex hormone binding globulin

TVS : Transvaginal sonography

UL : Upper intake level

VDR : Vitamin D receptor

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Protocol of Thesis

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Faculty of Medicine - Ain Shams University

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Faculty of Medicine - Ain Shams University

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INTRODUCTION

Infertility is a complex disorder with significant medical, psychosocial, and economic aspects **(Benyamini et al., 2005).**

Infertility has been defined by the World Health Organization (WHO) as the failure of a couple to achieve a clinical pregnancy after twelve months of regular intercourse without the use of contraception **(Zegers et al., 2009).**

The World Health Organization estimated that approximately 10-25% of couples have infertility disorder. Infertility affects about 80 million people across the world. Assisted reproductive technology (ART) is used to achieve pregnancy by artificial means **(Syiem et al., 2013).**

Thirty per cent of infertile couples worldwide are diagnosed with unexplained or idiopathic infertility and the problem is defined as the lack of an obvious cause for a couple's infertility and the females' inability to get pregnant after at least 12 cycles of unprotected intercourse or after six cycles in women above 35 years of age for whom all the standard evaluations are normal. The veracity of 'unexplained infertility' term has been challenged by many clinicians and researchers; they emphasize that the assignment of this title to an infertile couple is much dependent on the quantity, quality and nature of the applied diagnostic tests **(Gelbaya et al., 2014).**

Our inability to find the causes of couples' infertility does not mean that there is no cause for the disorder. Extensive research should be conducted on other possible causes of failed conception such as ovarian and testicular dysfunctions, sperm and oocyte quality, fallopian transport defects, endometrial receptivity, implantation failures, and endometriosis **(Hatasaka, 2011).**

Vitamin D has been well-known for its function in maintaining calcium and phosphorus homeostasis and promoting bone mineralization**(Holick, 2007).**Recent studies support the role of vitamin D in

human reproduction and suggest that vitamin D levels predict reproductive success following in vitro fertilization (IVF) **(Garbedian et al., 2013).**

Vitamin D receptors are found in various reproductive tissues, including ovarian and uterine tissue. Further evidence supporting an association between vitamin D and reproduction comes from studies of the vitamin D receptor **(Daftary et al., 2006).**

Vitamin D insufficiency affects almost 50% of the population worldwide **(Holick, 2007).**

The circulating level of the 25-(OH) vitamin D is the universally accepted indicator of vitamin D status **(Wolpowitz et al., 2006).**

The classification of vitamn D status varies in the literature **(Bikle, 2010)** and because the relation between vitamin D and fertility has only recently been investigated, no specific cut-off values have been referenced in the literature. However, a Canadian guideline defined vitamin D deficiency as levels below 25 nmol/L, insufficiency as levels between 25 and 74 nmol/L and sufficiency as levels of 75 nmol/L and greater **(Garbedian et al., 2013).**

Since 2013, the database of the US National Library of Medicine National Institutes of Health (Pub Med) has gained 2050 new publications about vitamin D and contains 62,427 articles regarding this subject. Research on the role of vitamin D in reproduction process modulation seems especially interesting; their conclusions presumably have a significant practical meaning in infertility treatment, a serious medical problem affecting up to 53 million people worldwide **(Filip et al., 2015).**

What is the role of cholecalciferol in human reproduction? Should its supplementation become a golden standard in fertility treatment, or do we still need more evidence on its effect? **(Filip et al., 2015)**

In a study with 84 infertile women undergoing IVF, women with higher levels of 25 (OH) vit D in follicular fluid and serum had significantly

higher clinical pregnancy rates following IVF, and high vitamin D levels were significantly associated with better parameters of controlled ovarian hyperstimulation **(Ozkan et al., 2010).**

In contrast, Aleyasin et al could not show a significant association between serum and follicular fluid 25 (OH) vitamin D levels and IVF outcomes in a study including 82 infertile women undergoing ART **(Aleyasin et al., 2011).**

Anifandis and co-workers investigated 101 women undergoing 101 IVF-intracytoplasmatic sperm injection (ICSI) cycles. In their study, women with a sufficient follicular fluid vitamin D status (25 (OH) vitamin D >30 ng/ml) had a poorer quality of embryos and significantly lower clinical pregnancy in comparison with women with deficient vitamin D status (follicular fluid 25 (OH) vitamin D <20 ng/ml) or insufficient (follicular fluid 25 (OH) vitamin D 20.1-30 ng/ml) **(Anifandis et al., 2010).**