TSH and AMH in Infertile Women

Thesis

Submitted for Partial Fulfillmentof Master Degree in
Obstetrics and Gynecology

By

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Haitham Hassan

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List of Abbreviations

ACTH	**:**	Adrenocorticotropic hormone
ACVR1	**:**	Activin A receptor, type I
AE-PCOS Society	**:**	Androgen Excess and Polycystic Ovary Syndrome Society
AES	**:**	Androgen Excess Society
AFC	**:**	Antral follicle count
Alk	**:**	Activin receptor-like kinase
AMH	**:**	Anti-Müllerian hormone
AMHR2	**:**	Anti-Müllerian hormone specific type 2 receptor
ANOV	**:**	Anovulation
ART	**:**	Assisted Reproductive Techniques
ASRM	**:**	American Society for Reproductive Medicine
AUC	**:**	Area under the curve
β	**:**	Regression coefficient
BMI	**:**	Body mass index
BMPR	**:**	Bone morphogenetic protein receptor
BMPs	**:**	Bone morphogenetic proteins
CAH	**:**	Congenital adrenal hyperplasia
CI	**:**	Confidence Interval
CL	**:**	Corpus luteum

CNS	**:**	Central nervous system
DF	**:**	Degree of freedom
DHEA-S	**:**	Dehydroepiandrosterone sulfate
DHT	**:**	Di-hydro-testosterone
DIT	**:**	Diiodotyrsine
DNA	**:**	Deoxyribonucleic acid
E_1	**:**	Estrone
E_2	**:**	Estradiol
ELISA	**:**	Enzyme-linked immunosorbent assay
ESHRE	**:**	European Society of Human Reproduction and Embryology
FSH	**:**	Follicle-stimulating hormone
GH	**:**	Growth hormone
GnRH	**:**	Gonadotropin-releasing hormone
GnRH-A	**:**	Gonadotrophin - releasing hormone analogue
HCG	**:**	Human chorionic gonadotropin
HMG	**:**	Human menopausal gonadotropin
HRP	**:**	Horseradish peroxidase
IBM	**:**	International Business Machines Corporation
ICSI	**:**	Intra-cytoplasmic sperm injection
IGF-1	**:**	Insulin-like growth factor-1

IGFBP-1	**:**	Insulin - like growth factor-binding protein-1
IgG	**:**	Immunoglobulin G
IR	**:**	Insulin resistance
IV	**:**	Intravenous
IVF	**:**	In Vitro Fertilization
IVM	**:**	In Vitro Maturation
J	**:**	Youden index
LH	**:**	Luteinizing hormone
MHPG	**:**	3-Methoxy-4-hydroxyphenylglycol
MIS	**:**	Müllerian-inhibiting substance
MS	**:**	Metabolic syndrome
MIT	**:**	Monoiodotyrosine
NIH	**:**	National Institutes of Health
OHSS	**:**	Ovarian **hyperstimulation** syndrome
OR	**:**	Odds ratio
PCO	**:**	Polycystic ovaries
PCOD	**:**	Polycystic ovary disease
PCOM	**:**	Polycystic ovary morphology
PCOS	**:**	Polycystic ovary syndrome
P-value	**:**	Probability value
RI	**:**	Resistance index
ROC	**:**	Receiver operating characteristic

R-Smads	**:**	Receptor - regulated small mothers against decapentaplegic proteins
SC	**:**	Subcutaneous
SD	**:**	Standard deviation
SE	**:**	Standard error
SHBG	**:**	Sex hormone-binding globulin
SMADs	**:**	Small mothers against decapentaplegic proteins
SPSS	**:**	Statistical Package for the Social Sciences
T3	**:**	Triiodothyronine
T4	**:**	Thyroxine
TAI	**:**	Thyroid autoantibodies
TBG	**:**	Thyroxine Binding globulin
TBOAb	**:**	Thyroid peroxidase antibodies
TBPA	**:**	Thyroxine binding prealbumin
Tg	**:**	Thyroglobulin
TgAb	**:**	Thyroglobulin antibodies
TGF-β	**:**	Transforming growth factor-beta
TMB	**:**	Tetramethylbenzidine
TRH	**:**	Thyrotropin-releasing hormone
TRβ2	**:**	Thyroid hormone receptor β2
TSH	**:**	Thyroid-stimulating hormone
TTR	**:**	Transthyretin

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Protocol of Thesis

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Introduction

Infertility is defined as the inability of a couple to achieve pregnancy over an average period of one year (in women under 35 years of age) or 6 months (in women above 35 years of age) of unprotected sexual intercourse. Infertility can be due to female, male reasons or both. It can be either primary or secondary ***(Cooper et al., 2010)***.

Thyroid dysfunction and autoimmune thyroiditis are known adverse risk factors for pregnancy as well as fertility, regardless of the presence of disease in women of reproductive age ***(Krassas et al., 2010)***. In particular, hypothyroid women are at an increased risk of menstrual disorders and infertility because of altered peripheral estrogen metabolism, hyperprolactinaemia and abnormal release of gonadotropin-releasing hormone ***(Krassas et al.,2010)***.

The prevalence of subclinical hypothyroidism characterized by aberrant high serum thyroid-stimulating hormone (TSH) levels with normal free thyroxin (FT4) levels in infertile women are reported to be approximately 20% and it is a primary cause of subfertility***(De Groot et al., 2012)***.

Indeed, average TSH levels in infertile women were reportedly higher than those in normal fertile women. And elevated serum TSH levels were associated with diminished ovarian reserve in infertile patients ***(Michalakis et al., 2011*)**. Moreover, although levothyroxine replacement therapy for subclinical hypothyroidism in infertile patients remains debatable, thyroxin supplementation may improve fertility to successful pregnancy***(Velkeniers et al., 2013)***.

This data suggests that hypothyroidism is strongly correlated with infertility ***(Velkeniers et al., 2013)***.

On the other hand, female fecundity decreases with increasing age, primarily because of decreased ovarian function. Anti-mullerian hormone (AMH) is a dimeric glycoprotein belonging to the transforming growth factor-beta (TGF-B) super family, which act on tissue growth and differentiation. It is produced by the granulosa cells from pre-antral and small antral follicles. Ovarian research after oophorectomy showed that serum AMH levels were closely correlated with the number of primordial follicles; therefore, AMH is a suitable biomarker of ovarian age in women of reproductive age ***(Hansen et al., 2011*)**.

Expectedly, ovarian function may be affected by impaired thyroid function, however this association has not been studied enough.

Aim of the Work

Research hypotheses:

In infertile women of reproductive age, serum TSH levels maybe elevated and serum AMH levels maybe decreased.

Research question:

In infertile women, is there any association between serum TSH levels and serum AMH levels?

Aim of the work:

The aim of this study is to evaluate the association between thyroid function and serum AMH levels.