

TSH and AMH in Infertile Women

Thesis

*Submitted for Partial Fulfillment of Master Degree in
Obstetrics and Gynecology*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لسبب أنك لا تعلم لنا
إلا ما علمتنا أنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

ACTH	: Adrenocorticotrophic hormone
ACVR1	: Activin A receptor, type I
AE-PCOS	: Androgen Excess and Polycystic Ovary
Society	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

List of Abbreviations

CNS	: Central nervous system
DF	: Degree of freedom
DHEA-S	: Dehydroepiandrosterone sulfate
DHT	: Di-hydro-testosterone
DIT	: Diiodotyrosine
DNA	: Deoxyribonucleic acid
E₁	: Estrone
E₂	: 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

List of Abbreviations

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 β 2
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 thyroxine (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.