

SERUM INTERLEUKIN-6 AND POLYCYSTIC OVARY SYNDROME

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَأَنْزَلَ اللَّهُ
عَلَيْكَ الْكِتَابَ
وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ
وَكَانَ فَضْلُ
اللَّهِ عَلَيْكَ
عَظِيمًا

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List of Abbreviations

Abbrev.	Meaning
ACOG	American College of Obstetrics and Gynecology
ACTH	Adrenocorticotrophic Hormone
Arg	Argenine
ASRM	American Society for Reproductive Medicine
atRA	All-trans-Retinoic Acid
AUC	Area under the curve
BMI	Body Mass Index
CC	Clomiphene Citrate
CD	Cluster of Differentiation
2 D	2 dimensions
DHEAS	Dihydroepiandrosterone Sulphate
DM	Diabetes Mellitus
E	Estrogen
ELISA	Enzyme Linked Immunosorbant Assay
ESHRE	European Society for Human Reproduction and Embryology
FSH	Follicle Stimulation Hormone
Gly	Glycine
GnRH	Gonadotrophin Releasing Hormone
Gp130	Glycoprotein 130
hCG	Human Chorionic Gonadotropins
hMG	Human menopausal gonadotropins
HOMA IR	Homeostatic model assessment for insulin resistance
17-HP	17- Hydroxyprogesterone
HS	Highly significant
IL-6	Interleukin-6
IL-6R	Interleukin-6 receptor

List of Abbreviations (Cont...)

Abbrev.	Meaning
IR	Insulin Resistance
IU/L	International Unit per liter
IVF	In Vitro Fertilization
IVM	In Vitro Maturation of oocytes
JAKs	Janus Kinases
LH	Luteinizing Hormone
LOD	Laparoscopic Ovarian Drilling
mFG	Modified Ferriman-Gallwey score
MHz	Megahertz
mm	Millimeter
NCAH	Non- classic Congenital Adrenal Hyperplasia
NICHD	National Institute of Child health and Human Development
NIH	National Institute of health
nmol/L	Nanomol per liter
NS	Non significant
21-OH	21- hydroxylase
OHSS	Ovarian Hyperstimulation Syndrome
p	Propability
P	Progesterone
PCOS	Polycystic Ovary Syndrome
pg/ml	Picogram per millileter
pmol/L	Picomol per liter
-PV	Negative predictive value
+PV	Positive predictive value

List of Abbreviations (Cont...)

Abbrev.	Meaning
RIA	Radioimmune Assay
ROC	Receiver operator characteristic curve
S	Significant
SD	Standard deviation
Sgp130	Soluble glycoprotein 130
SHBG	Sex Hormone Binding Globulin
sIL-6R	Soluble Interleukin-6 Receptors
STATs	Signal Transducers and Activators of Transcription
T	Testosterone
TSH	Thyroid Stimulating Hormone
TV-US	Trans-Vaginal Ultra-Sound
WHR	Waist to hip ratio

INTRODUCTION

The polycystic ovary syndrome (PCOS) is the most common hormonal disorder in young women, estimated to affect 5-10% of women through and beyond their reproductive age (*Crosignani and Nicolosi, 2001*).

PCOS is characterized by chronic anovulation or infrequent ovulation, obesity, hirsutism, hyperandrogenism and numerous follicular cysts in enlarged ovaries. PCOS is the leading cause of anovulatory infertility among premenopausal women. Such patients are also at increasing risk of obesity, insulin resistance, type 2 diabetes mellitus, premature atherosclerosis and endometrial cancer (*Dasgupta and Reddy, 2008*).

Ovarian macrophages play a paracrine role in the regulation of ovarian function through the local secretion of regulatory molecules. Numerous studies have shown that a variety of cytokines such as interleukin-6 (IL-6) can exert profound effects on ovarian function and probably also on reproductive processes (*Salmassi et al., 2001*).

Proper follicle development is dependent on the proper cytokines and growth factors milieu. Cytokines are small proteins that act locally on immune system and the surrounding tissues (*Wu et al., 2004*).

These cytokines impact many aspects of ovarian functions including follicle growth and differentiation, ovulation, corpus luteum formation and function (**Wu et al., 2004**).

PCOS women undergoing IVF were noted to have higher serum concentration of IL-6 during ovarian suppression than women undergoing IVF for male factor infertility. They also have higher serum and follicular concentrations of IL-6 at the time of ovum retrieval (**Amato et al., 2003**).

AIM OF THE WORK

The aim of the study is to investigate the association between serum IL-6 concentration and polycystic ovary syndrome.

Chapter 1

POLYCYSTIC OVARY SYNDROME

1- Historical background:

In 1935, Irving F. Stein and Michael L. Leventhal first described a symptom complex associated with anovulation. They described seven patients (four of whom were obese) with amenorrhea, hirsutism, infertility. After conservative therapies failed, the women underwent laparotomy, which revealed enlarged ovaries with thickened tunica and multiple (20-100 per ovary) follicle cysts. Stein and Leventhal developed the wedge resection after they observed that several of their amenorrheic women menstruated after ovarian biopsies. They reasoned that the thickened tunica was preventing the follicles from reaching the surface of the ovary. The condition was for a long time called the Stein- Leventhal syndrome. After bilateral wedge resection, removing one-half to three-fourth of each ovary, all 7 patients regain menstruation and two of them became pregnant (*Stein and Leventhal, 1935*).

2- Definition

a- Basics:

It should be recognized that polycystic ovary syndrome (PCOS) is still a "syndrome", namely a