EVALUATION OF SERUM IL-23 LEVEL IN ACTIVE, STABLE AND NARROW BAND ULTRAVIOLET B TREATED VITILIGO

Thesis

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Omar Ala Dawod

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List of Abbreviations

Abb.	Full term

AA**.....** *Arachidonic acid*
ACE**.....** *Angiotensin – Converting Enzyme*
AHA**.....** *American heart association*
AICAR**.....** *Aminoimidazole -4- carboxamide ribonucleotide*
AIDS **.....** *Acquired immunodeficiency syndrome*
AMPK**.....** *Adenosine monophosphate kinase*
AMPs**.....** *Antimicrobial peptides*
AP-1**.....** *Activator protein -1*
APCs **.....** *Antigen presenting cells*
AS**.....** *Ankylosing spondylitis*
BAT **.....** *Brown adipose tissue*
BCG**.....** *Balillus Calmette-Guerin*
BMI **.....** *Body mass index*
BP**.....** *Blood pressure*
BSA **.....** *Body surface area*
CB-1 **.....** *Cannabinoid-1 receptor*
CBD**.....** *Cytokine binding domains*
CD **.....** *Cluster of differentiation*
CVD**.....** *Cardiovascular disease*
DCs**.....** *Dendritic cells*
DLQI**.....** *Dermatology Life Quality Index*
DM**.....** *Diabetes Mellitus*
DPP**.....** *Diabetes prevention program*
EAE**.....** *Experimental autoimmune encephalomyelitis*
EDTA **.....** *Ethylene diamine tetra-acetic acid*
EGF**.....** *Epidermal growth factor*
EGF-R **.....** *Epidermal growth factor receptor*
ELIZA **.....** *Enzyme linked immunosorbant assay*
GBP-28**.....** *Gelatin binding protein-28*

List of Abbreviations (Cont...)

Abb.	Full term
GLUT4	*Glucose transporter type 4*
GM-CSF	*Granulocyte macrophage colony stimulating factor*
HDL	*High density lipoprotein*
HEV	*High Endothelial Venules*
HIV	*Human Immunodeficiency Virus*
HMW	*High molecular weight*
IBD	*Inflammatory bowel disease*
ICAM	*Intercellular adhesion molecule*
Ig	*Immune globulin*
IGF-1	*Insulin growth factor-1*
IGT	*Impaired glucose tolerance*
IL	*Interleukin*
ILs	*Interleukins*
INF	*Interferon*
iNOS	*Inducible nitric oxide synthase*
IR	*Insulin resistance*
kDa	*Kilo Dalton*
LC	*Langerhans' cell*
LCAT	*Lecithin cholesterol acyltransferase*
LDL	*Low density lipoprotein*
LFA	*Lymphocyte functional antigen*
LPS	*Lipopolysaccharide*
LT	*Leukotriens*
MCA	*Methyl cholanthrene-A*
MCP-1	*Monocyte chemotactic protein-1*
MDA	*Malondialdehyde*
MHC	*Major histocompatibility complex*
MITF	*Microphthalmia-associated transcription factor*
MMPs	*Matrix metallopeptidases*

List of Abbreviations (Cont...)

Abb.	Full term
mRNA	*Messenger ribonucleic acid*
MS	*Metabolic syndrome*
MTX	*Methotrexate*
NCEP	*National cholesterol education program*
NF-AT	*Nuclear factor of activated T cell*
NF-κB	*Nuclear Factor- κB*
NGF	*Nerve growth factor*
NK	*Natural killer*
NO	*Nitric oxide*
NSAIDS	*Non-Steroidal Anti-inflammatory Drugs*
PAI-1	*Plasminogen activator inhibitor-1*
PASI	*Psoriasis area and severity index*
PGA	*Physician Global Assessment*
PLE	*Polymorphic light eruption*
PPAR	*Peroxisome proliferator- activated receptor*
PsA	*Psoriatic arthritis*
PSORS	*Psoriasis Susceptibility*
PUVA	*Psoralen + UVA*
RA	*Rheumatoid arthritis*
Scf	*Stem cell factor*
SOD	*Superoxide Dismutase*
SP	*Substance P*
T regs	*T regulatory cells*
TACE	*TNFα convertase enzyme*
TAS	*Total Antioxidant Status*
Tc-1	*T cytotoxic -1*
TCR	*T cell receptor*
TG	*Triglycerides*
TGF-β	*Transforming growth factor-β*

List of Abbreviations (Cont...)

Abb.	Full term
Th	*T-helper*
TLR	*Toll like receptor*
TNFR	*Tumor necrosis factor receptor*
TNFSF	*Tumor necrosis factor superfamily*
TNF-α	*Tumor necrosis factor-alpha*
TZD	*Thiazolidinedione*
UVA	*Ultraviolet A*
UVB	*Ultraviolet B*
VASI	*Vitiligo area scoring index*
VCAM	*Vascular cell adhesion molecule*
VEGF	*Vascular endothelial growth factor*
VIDA	*Vitiligo disease activity score*
VIP	*Vasoactive intestinal peptide*
vit	*Vitiligo*
VPF	*Vascular permeability factor*
WAT	*White adipose tissue*
WC	*Waist circumference*
WHO	*World Health Organization*

INTRODUCTION

Vitiligo is an acquired depigmentary disorder characterized by the loss of functioning epidermal melanocytes and affects more than 0.5–1% of the worldwide population with devastating psychological and social consequences ***(Feily, 2014).*** The exact pathologic mechanism has not been clarified yet; however, the autoimmune hypothesis is the most widely accepted explanation ***(Shin et al., 2010).***

Vitiligo has been classified according to the clinical ground into two major forms, namely segmental vitiligo (S.V.) and non-segmental vitiligo (N.S.V.), the latter includes several variants (generalized, acro facial and universal), non segmental vitiligo typically evolves over time in both distribution and extension patterns ***(Taieb and Picardo, 2007).***

Peripheral blood and skin biopsies of patients with vitiligo showed that T cells, mononuclear cells, pro-inflammatory cytokines and autoanti bodies can damage melanocytes ***(Sandoval-Cruz et al., 2011).*** Peripheral lesional cytotoxic T cells seem to be responsible for the depigmentation process which may produce targeted autoimmune tissue destruction ***(Zamani et al., 2001).***

A significant change of epidermal cytokines in involved skin of patients with vitiligo compared with uninvolved skin and skin of healthy controls has been described ***(Kim et al.,***

2011)**,** among these proinflammatory cytokines is IL-23 which is a member of IL-12 family that activates the effector function of T helper 17 (TH 17) cells to promote the inflammatory responses, this cytokine induces the production of TH17 cells so it was thought that it mediates autoimmunity by secretion of IL17 family, it has been established that IL-23 is essential for the development of autoimmune diseases, including psoriatic skin inflammation, inflammatory bowel diseases auto immune diabetes and others ***(Croxford et al., 2012).***

In patients with vitiligo increased levels of IL-17 (which is mediated by IL-23) in serum was observed suggesting that IL-17 is participating in the immune response in early onset of the disease ***(Duvallet et al., 2011)*****,** for this reason IL-23/TH-17 was considered as a relevant target in treatment of auto immune diseases and the biological agents blocking IL-23 or IL-17 are currently being developed, Ustekinumab is a mono clonal anti body targeting the common P40 subunit of IL-23 and IL-12 ***(Toussirot, 2012).***

Phototherapy is the therapeutic use of ultraviolet irradiation without exogenous photosensitizer ***(Rai and Srinivas, 2007).***

It is thought that its capability to induce T cell apoptosis is an indicator of clinical efficacy, furthermore, keratinocytes may be influenced to release other unidentified cytokines and factors, which suggests that UVB functions as an immune modulator, which may support the theory of autoimmune component in the pathogenesis of vitiligo ***(Noborio et al., 2006).***