PSORIASIS AND INSULIN RESISTANCE

Thesis
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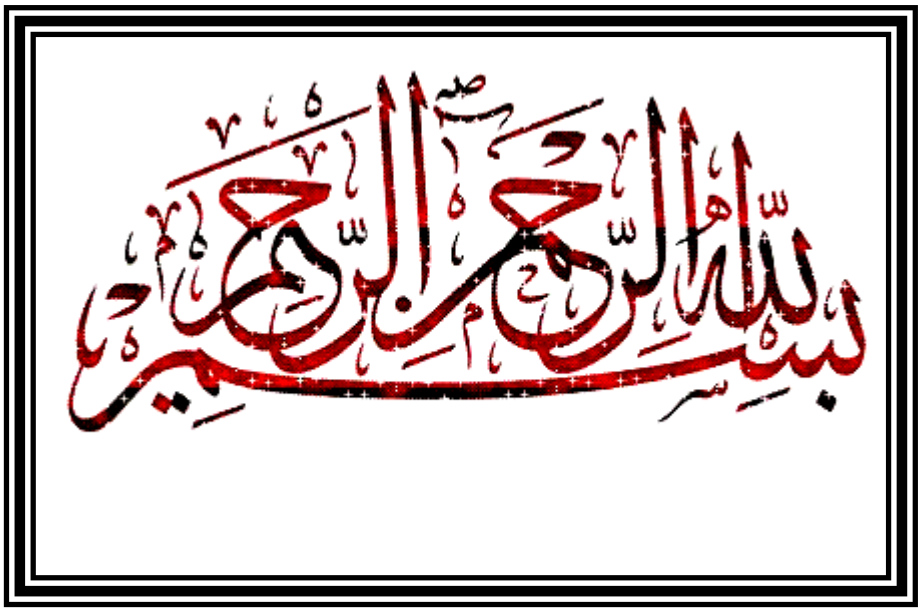
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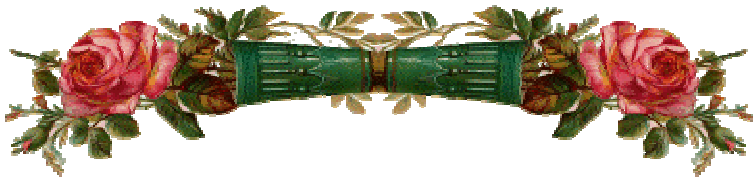

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LIST OF ABBREVIATIONS

α:	Alpha.
β:	Beta.
γ:	Gamma.
<:	Less than.
>:	More than.
%:	Percent.
^{o}c:	Degree Celsius.
µg:	Microgram.
µM:	Micromole.
µU:	Micro unit.
2 hpp:	2 hours postprandial blood glucose level.
A.A:	Arachidonic acid.
ADA:	American Diabetes Association.
ANOVA:	Analysis for variances.
APC:	Antigen presenting cell.
BMI:	Body mass index.
BSA:	Body surface area.
cAMP:	Cyclic adenosine monophosphate.
CLA:	Cutaneous lymphocyte antigen.
CRP:	C-reactive protein.
CVD:	Cardiovascular disease.
DCs:	Dendritic cells.
dl:	Disi Liter.
DM:	Diabetes mellitus.
ECT:	Euglycemic clamp technique.
EGF-R:	Epidermal growth factor receptor.

ELISA: Enzyme Immunoassay.

FBG: fasting blood glucose level.

FDA: Food and Drug Administration.

GLUT: Glucose transporter.

GM-CSF: Granulocyte macrophage colony stimulating factor.

HDL: High density lipoprotein.

HIV: Human immunodeficiency virus.

HLA: Human leucocyte antigen.

HOMA: Homeostasis model assessment.

HSD: Hydroxysteroid dehydrogenase.

ICAM: Intercellular adhesion molecule.

IFG: Impaired fasting glucose.

IFN: Interferon.

IGF Insulin-like growth factor.

IGFBP: Insulin-like growth factor binding protein.

IGR: Impaired glucose regulation.

IGT: Impaired glucose tolerance.

IGT-2hpp: Impaired glucose tolerance-2 hours postprandial.

IL: Interleukin.

IMT: Intima-media thickness.

IR: Insulin resistance.

IRS: Insulin resistance syndrome.

ITT: Insulin tolerance test.

KC: Keratinocyte.

Kg: Kilogram.

KGF: Keratinocyte growth factor.

LDL: Low density lipoprotein.

LFA: Leucocyte function associated antigen.

MAP: Mitogen-activated protein.

MCP: Monocyte chemoattractant protein.

Mg: Milligram.

Mg/dl: Milligram per decileter.

MHC: Major histocomptability complex.

Mmol: Mille moll.

MS: Multiple sclerosis.

MTX: Methotrexate.

NGF: Nerve growth factor.

NHL: Non-Hodgkin's lymphoma.

NIDDM: Non-insulin-dependent diabetes mellitus.

OGTT: Oral glucose tolerance test.

PAI: Plasminogen activator inhibitor.

PASI: Psoriasis area and severity index.

PI3K: Phosphatidylinositol-3'-kinase.

PLE: Polymorphic light eruption.

PPAR: Peroxisome proliferator activated receptor.

PsA: Psoriatic arthritis.

PSORS: Psoriasis susceptibility locus.

PUFA: Polyunsaturated fatty acid.

QOL: Quality of life.

RA: Rheumatoid arthritis.

RF: Rheumatoid factor.

SAA: Serum amyloid A.

SD: Standard deviation.

SP: Substance P.

TGF: Transforming growth factor.

Th: T helper.

TNF: Tumor necrosis factor.

USA: United states of America.

VCAM: Vascular cell adhesion molecule.

VDR: Vitamin D receptor.

VEGF: Vascular endothelial growth factor.

VLA: Vascular lymphocytic antigen.

WHO: World Health Organization.

Ys: Years.

INTRODUCTION

Psoriasis is a chronic and debilitating inflammatory disease associated with serious co-morbidities and causes a significant impact on the patient's quality of life *(Gottlieb et al., 2008)*.

Psoriatic patients have an increased prevalence of the core components of metabolic syndrome, including obesity, dyslipidemia, insulin resistance, diabetes mellitus and cardiovascular disease. Persistent low-grade inflammation with secretion of proinflammatory cytokines favors the development of insulin resistance and metabolic syndrome. In addition, biochemical and immunologic mechanisms may play a role *(Cohen et al., 2008)*.

High prevalence of diabetes mellitus (DM) in patients with psoriasis has long been recognized *(Hilal et al., 2007)*. It is generally accepted that the emergence of type II DM is preceded by a stage of impaired glucose tolerance (IGT). Many studies have shown that IGT individuals are resistant to the action of insulin and that the progression from IGT to type II DM is associated with a decline in beta-cell function with additional worsening of peripheral insulin resistance *(Kahn, 2001)*.

Insulin resistance (IR) affects 10-25% of the general population. It is often considered a central component of metabolic syndrome that significantly increases the risk of cardiovascular morbidity and mortality and plays an important role in the pathophysiology of type II diabetes mellitus *(James et al., 2004)*.

The association between psoriasis and DM is possibly related to the presence of insulin resistance in psoriatic patients. Recognizing insulin resistance and elements of the metabolic

syndrome in psoriatic patients together with changing in life habits and appropriate drug therapy could be of great value in reducing the risk of cardiovascular morbidities and type II diabetes mellitus *(Puig, 2007)*.

AIM OF THE WORK:

The aim of our study is to detect the insulin resistance (IR), impaired glucose tolerance (IGT) in psoriatic patients and their possible relations to the clinical variants, duration and severity of psoriasis.

CHAPTER I

An Overview on Psoriasis

Psoriasis is a common, chronic inflammatory skin disease characterized by spontaneous remissions and exacerbations. The lesions are characterized by circumscribed, dry, erythematous plaques of various sizes covered by silvery white scales. The scalp, nails, extensor surfaces of the limbs, umbilical region and sacrum are sites of predilection. Lesions are usually symmetrical and develop slowly but may be eruptive, with sudden onset of numerous guttate (drop-like) lesions *(James et al., 2006)*.

Various studies showed that psoriasis affects approximately 0.6-4.8% of the general population (*Gelfand et al., 2005)*.

Two peaks for the onset of psoriasis have been described: a large peak between the ages of 20-30 years, and a small peak between 50-60 years *(Bowcock and Barker, 2003)*. There is no sex predilection, although, significant female preponderance in the palmoplantar pustular type was found by *Griffiths et al. (2000)*.

Clinical Variants:

Chronic plaque psoriasis is the most common variant of psoriasis vulgaris. It is characterized by being symmetrically distributed, well demarcated from adjacent symptomless skin, erythematous and covered by white-silvery scales. The plaques are predominantly located on the elbows, knees, lower back, umbilicus hands and feet. The genetalia are involved in up to 30% of patients *(Nickoloff and Nestle, 2004)*.

Guttate psoriasis appears particularly in children and young adults after acute streptococcal infections. Lesions are varying from 2mm-1cm in diameter which is rounded or slightly oval, scattered particularly on the trunk and proximal part of the limbs *(Peter and Joost, 2008)*.

Pustular psoriasis is classified into two main groups: Generalized and localized forms. Disseminated deep-red erythematous areas and sterile pustules characterize generalized pustular psoriasis, which may merge to extensive lakes of pus. In contrast, there are two localized variants termed palmoplantar pustulosis and acrodermatitis continua suppurativa *(Michael et al., 2005*).

Erythrodermic psoriasis is a variant of psoriasis characterized by generalized erythema and scaling involving more than 90% of the whole body surface area. It may present suddenly or as a result of withdrawal of potent topical or oral corticosteroids or methotrexate. Furthermore, it is usually precipitated by infection, hypocalcaemia and antimalarial drugs (*Sterry and Muche, 2003)*.

Special localizations include; flexural psoriasis, scalp, mucous membrane lesions, psoriatic arthritis and nail changes *(Peter and Joost, 2008)*.

Flexural (inverse) psoriasis is characterized by shiny sharply demarcated erythema with no scaling. It involves the body folds; groins, vulva, axillae, sub-mammary folds and gluteal cleft.

Scalp psoriasis is often associated with itching and it affects heavily the quality of life of the patients. The scalp is one of the common sites affected in psoriasis. The lesions tend to advance to