# بسم الله الرحمن الرحيم

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بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

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# Analysis of Serum Chemerin Level in Acanthosis Nigricans Patients: A Case Control Study

Thesis

Submitted for Partial Fulfillment of Master Degree
in **Dermatology, Venereology And Andrology**

By

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Menna Mohamed El Zawahry

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# List of Abbreviations

| Abb. | Full term |
|---|---|
| AN | Acanthosis Nigricans |
| ATP | Adenosine triphosphate |
| AV | Acne vulgaris |
| CMKLR1 | Cognate receptor chemokine-like receptor-1 |
| DEJ | Dermoepidermal junction |
| FGFR3 | Fibroblast growth factor receptor 3 |
| HCC | Hepatocellular carcinoma |
| HIV | Human immunodeficiency virus |
| HOMA | Homeostatitc model assessment |
| HS | Hidradenitis suppurativa |
| IDF | International Diabetes Federation |
| IGF-1 | Insulin-like growth factor-1 |
| IGF-1Rs | Insulin-like growth factor 1 receptors |
| IGFBPs | Insulin-like growth binding proteins |
| IR | Insulin resistance |
| LPS | Lipopolysaccharide |
| METS | Metabolic syndrome |
| MHO | Metabolically healthy obese |
| mtDNA | Mitochondrial DNA |
| NCEP | National Cholesterol Education Program |
| PCOS | Polycystic ovarian syndrome |
| RARRES2 | Retinoic Acid Receptor Responder 2 |
| T2D | Type 2 diabetes |
| T2D | Type 2 diabetes mellitus |
| TGF | Transforming growth factor |
| TIG2 | Tazarotene-induced gene 2 |
| TZD | Thiazolidinedione |
| VCAM-1 | Vascular cell adhesion molecule-1 |
| WAT | White adipose tissue |

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# INTRODUCTION

Acanthosis Nigricans (AN) is a dermatological condition that has been recognized for more than a hundred years. It is characterized by thickened, hyperpigmented plaques, typically of the intertriginous surfaces and neck. Common in some populations, its prevalence depends on race ***(Higgins et al., 2008)***.

The association of AN, skin tags, diabetes mellitus due to insulin resistance, and obesity in children and adults represents a well-defined syndrome. Apparently, the only AN predictive factor are hyperinsulinism and severe obesity, not age or pubertal stage ***(Guran et al., 2008).*** The recent rise in human obesity is caused by increased energy intake and decreased energy expenditure that results in a massive increase in adipose tissue that is generally harmful to health. Indeed, the rise in human obesity is closely associated with an increase in diseases such as type 2 diabetes (T2D), cardiovascular disease, hepatic steatosis, airway disease, neurodegeneration, biliary disease, and certain cancer **(*Hotamisligil, 2006).***

Various benign forms of AN have been identified in which the disorder may be inherited as a primary condition or associated with various underlying syndromes, such as obesity as it is the most common cause for AN, that's what called pseudo AN, or it may appear as an adverse effect of

several medications (drug-induced AN). In other instances, AN may occur in association with an underlying malignant tumor (paraneoplastic type) **(*Phiske, 2014).***

The endocrine origin of this condition is beyond doubt. Insulin and insulin-like growth factor-1 (IGF-1), and their receptors on keratinocytes are obviously involved in the paradox', which associates better survival and fewer cardiovascular events in patients with mildly elevated BMI afflicted with chronic diseases (***Paul, 2007).***

Metabolic syndrome is the aggregate of clinical conditions comprising central and abdominal obesity, systemic hypertension, insulin resistance or T2D, and atherogenic dyslipidemia ***(Naldi and Mercuri, 2010)***.

It has been demonstrated that there is a dysregulated adpokine balance as an important link between inflammation, metabolic syndrome and consequential disorders ***(Wolk and Sabat, 2016)***.

Obesity has become the major health hazard of modern world and has become now a truly global problem due to the spread of the western lifestyle. Excess energy intake and concomitant obesity are the major drivers of this syndrome ***(Sakalyen, 2018)***.

Chemerin is an adipocytes-secreted protein with autocrine / paracrine roles on adipose development and

function as well as endocrine roles in metabolism and immunity. It can regulate adipocytes differentiation and stimulate chemotaxis of dendritic cells and macrophages ***(Fatima et al., 2014)***. Following prochemerin secretion, protease-mediated generation of chemerin isoforms with a range of biological activities is a key regulatory mechanism controlling local, context-specific chemerin bioactivity. Together, experimental and clinical data indicate that localized and/or circulating chemerin expression and activation are elevated in numerous metabolic and inflammatory diseases including, psoriasis, metabolic syndrome and cardiovascular disease ***(Zhou et al., 2019)***.

Chemerin has been linked to adiposity and insulin resistance which are the common characteristics of AN. These elevations are positively correlated with deleterious changes glucose, lipid, and cytokine homeostasis, and may serve as a link between obesity, inflammation and other metabolic disorders ***(Rourke et al., 2012).***

# AIM OF THE WORK

The aim of the study is assessment of serum concentrations of Chemerin level in patients with AN in comparison to the healthy control individuals, as well as evaluation of a possible correlation between chemerin concentrations and metabolic syndrome components.

# Chapter (1)

# ACANTHOSIS NIGRICANS

Acanthosis Nigricans (AN) is a common but most often neglected disorder affecting the skin. Though commonly used, the term Acanthosis nigricans is a misnomer, as acanthosis which means thickening of stratum spinosum is not seen in majority of cases on histopathology. While the term nigricans means black implies the darkening of skin which is seen in this disorder. Being asymptomatic consultation is seeked only for cosmetic purposes. Its importance lies in its association with many underlying systemic disorders, of which it can be an early warning sign. So, it is rather poorly defined as a dermatological disease by itself and more as a common dermatological manifestation of systemic disorders ***(Pardeshi et al., 2020).***

The early lesions may be erythematous and pruritic, mimicking an inflammatory psoriasiform dermatitis. Older lesions turn to verrucous or papillomatous darkly pigmented plaques ***(Karadağ et al., 2018).***

Cutaneous involvement is localized but not well circumscribed, since it blends imperceptibly into surrounding skin at the edges. Lesions usually develop in the flexures, especially the nape (Fig. 1a), the axilla (Fig. 1b), the side of the neck, the groin and anogenital areas.