

# Relation of Acanthosis Nigricans to Glycated Hemoglobin (HbA1c) Test and Lipid Profile among Iraqis

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**Abstract:** *Acanthosis Nigricans is a skin disorder characterized by hyperpigmentation, hyperkeratosis and papillomatosis with relationship to insulin resistance and metabolic changes. The aim of study to evaluate the role of acanthosis nigricans as a marker of Diabetes Mellitus and abnormal lipid profile by studying its relationship with age, ethnicity, anthropometry and other risk factors for T2DM in the Iraqi population. This study is a cross sectional study conducted in Dermatology Consultancy Clinic of Salahaldin General Hospital in Tikrit city during the period from 1<sup>st</sup> of November, 2018 to 31<sup>st</sup> of May, 2019 on samples of 50 patients with acanthosis nigricans and sample of 50m healthy adults were selected as controls. The acanthosis nigricans was diagnosed by the researcher clinically by clinical history and distinctive examination findings. Glycated hemoglobin and Lipid profile were assessed for study participants. Mean serum triglyceride of acanthosis nigricans patients was significantly higher than the mean serum triglyceride of controls (p=0.01). Mean low density and very low density lipoproteins of acanthosis nigricans patients were significantly higher than mean that for controls. Although both of glycated hemoglobin levels for acanthosis nigricans patients and controls were within normal range; but glycated hemoglobin mean of acanthosis nigricans patients was significantly higher than that for controls (p<0.001). In conclusion. The acanthosis nigricans is a common predictor for metabolic disorders like diabetes mellitus.*

**Keywords:** Acanthosis nigricans, Metabolic disorders, Diabetes mellitus, Lipid profile

## 1. Introduction

Acanthosis Nigricans (AN) is a disorder of the skin characterized by hyperpigmentation, hyperkeratosis, and papillomatosis, presenting as darkish blackish- brown, velvety lesions most often on the back of the neck, but also on other areas of the body, especially those that are prone to perspiration or friction (figure 1). AN has been associated with rare, genetic defects in insulin action, i.e., Type A insulin resistance and internal malignant neoplasms, especially adenocarcinomas. The increase in circulating insulin levels manifested in hyperinsulinemia results in the binding and stimulation of insulin receptors and growth factor-1 receptors on keratinocytes and dermal fibroblasts. Thus, AN is a visible, clinical marker of hyperinsulinemia [1].

Previously misdiagnosed as “Addison’s disease, “Acanthosis Nigricans is manifested by dark, raised skin in areas such as the axilla, neck, knuckles, elbows, and knees and is believed to result from hyperinsulinemia and can be easily recognized by the dark, velvety plaques of body folds seen around the neckline or in the axilla of children who have greater body weight and fat mass, higher serum insulin levels and lower insulin sensitivity”[2].

The presence of AN is a marker for the risk factor of hyperinsulinemia. “Hyperinsulinemia leads to binding of insulin-like growth factor (IGF) receptors on keratinocytes and fibroblasts resulting in hyperplasia of the skin”[3].

Curth classified AN into malignant, benign, and syndromic or pseudo AN. Hernandez-Perez proposed more simplified

classification: simple AN not related to malignancy and paraneoplastic AN.

Burke ET AL. classified AN according to the severity on a scale of 0-4 based on how many areas are affected. This scale is easy to use, having a high inter-observer reliability that correlates with fasting insulin and body mass index (BMI). [4]

AN may be diagnosed on the basis of thorough clinical evaluation, identification of characteristic physical findings, a complete patient history including medication history, a thorough family history, and various specialised tests. The age at detection will vary, depending upon the form of AN present and on other factors.

There is no specific treatment for AN.

In individuals with skin changes that suggest AN, diagnostic assessment may include various laboratory tests. Examples are the glucose tolerance test and the glycated haemoglobin (*HbA1c*) test. Additional laboratory studies or other specialized tests may also be utilized in diagnosis in order to help detect or rule out certain other underlying disorders – including a number of endocrine and autoimmune conditions – that may be associated with AN. In addition, in some instances, particularly where the patient presents with signs suggestive of malignant AN, testing may include biopsy and microscopic evaluation of small samples of skin tissue affected [5, 6].

Treatment is directed towards the specific symptoms that are apparent in each individual. It should be borne in mind that such treatment may require the coordinated efforts of a team

of medical professionals. Correcting the underlying disease improves the skin symptoms.



**Figure 1:** (a) Characteristic dark, coarse, thickened skin with a velvety texture of Acanthosis Nigricans (AN). (b) AN of the axillae with skin tags.

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## 2. Patients and Methods

This study is a cross sectional study conducted in Dermatology Consultancy Clinic of Salahaldin General Hospital in Tikrit city during the period from 1<sup>st</sup> of November, 2018 to 31<sup>st</sup> of May, 2019.

**Inclusion criteria:** Adults (age>18 years);

**Exclusion criteria:** ‘Melasma’ ‘Pigmented contact dermatitis’ Lichen planus pigmentosus ‘Poikiloderma of civatte’ ‘Pigmentary demarcation lines’ ‘Post inflammatory pigmentation’ ‘Topical/systemic drug induced pigmentation’ ‘Congenital/nevoid’ ‘Known diabetes mellitus’ Polycystic ovarian disease.

A sample of 50 patients with Acanthosis Nigricans presented to Dermatology Consultancy Clinic of Salahaldin General

Hospital was selected after eligibility to inclusion and exclusion criteria. A sample of 50 healthy adults was selected as controls. The data was collected by researcher from the study participants directly and filled in a prepared questionnaire.

AN patients and control healthy persons fasting status was determined on arrival after which weights, heights, WC, and BP were taken. then had their blood tested for S. cholesterol, S.TG, and other lipid profiles tests and A1c. After completion of all anthropometric measures and blood tests. Subjects completed the demographic questionnaire.

General physical examination was done with special emphasis on height, weight, body mass index (**BMI**) calculated by the formula: weight (in kg)/ (height in m) [2].

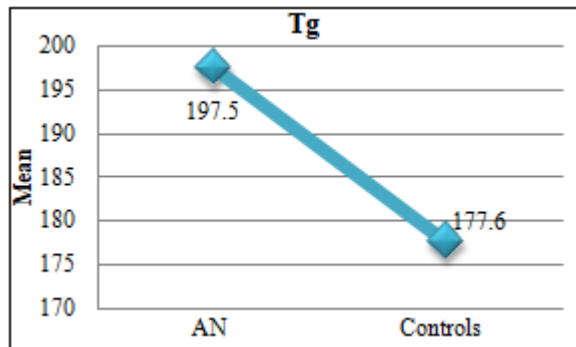
The Acanthosis Nigricans was diagnosed by the researcher clinically by clinical history and distinctive examination findings. A sample of 5 ml blood was drawn from each study participant 4 ml collected in plane tube then let stand for about 20 – 30 minute to clot formation and centrifuged by using macro-centrifuge for about (5- 15) minutes on speed of 3000 rpm then fresh non hemolysis serum collected and kept in deep freeze (-20<sup>0</sup>C) for biochemical investigations whereas 1 ml in EDTA tube for Hba1c test. The investigations were done in Laboratory of Salahaldin General Hospital and private laboratories in Tikrit city. The researcher and supervisor completed treatment of AN patients.

All study participants' data entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 20 was used.

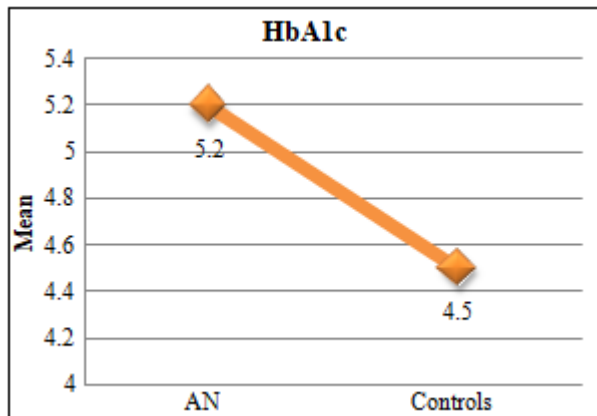
## 3. Results

No significant differences were observed between AN patients and controls regarding age (p=0.8) and gender (p=0.7). A significant difference was observed between AN patients and controls regarding occupation (p=0.02). No significant differences were observed between AN patients and controls regarding smoking (p=0.8), waist circumference (p=1.0), BMI (p=0.3) and blood pressure (p=0.8). No significant differences were observed between AN patients and controls regarding serum cholesterol means (p=0.1) and HDL means (p=0.2). Mean serum triglyceride of AN patients was significantly higher than mean serum triglyceride of controls (p=0.01). Mean LDL of AN patients was significantly higher than mean LDL of controls (p=0.01). (Figures 2)

Mean VLDL of AN patients was significantly higher than mean VLDL of controls (p=0.01). Although both of HbA1c levels for AN patients and controls were within normal range; but mean HbA1c mean of AN patients was significantly higher than HbA1c of controls (p<0.001).(figur



**Figure 2:** Distribution of Tg means according to AN cases and controls



**Figure 3:** Distribution of HbA1c means according to AN cases and controls

#### 4. Discussion

Present study showed that mean levels of triglycerides, LDL and VLDL of AN patients were significantly higher than controls. This finding is similar to results of Phiske study in India which reported an elevation in serum triglyceride level of patients with acanthosis nigricans[7].

Current study also found a significantly higher HbA1c level among acanthosis nigricans patients in comparison to controls ( $p < 0.001$ ). This finding is similar to results of Rafalson et al<sup>1</sup> study in USA which stated that acanthosis nigricans is accompanied by 50-100% risk of developing diabetes mellitus and poor glycemic control. Studying demographic characteristics of AN patients in present study showed that mean age of AN patients was 39.4 years. This finding is similar to results of Sharquieet. al.[8] study in Iraq which found that mean age of AN patients in Baghdad was 39 years.

Current study showed that male AN patients were more than females with male to female ratio as 6.1:1. This finding is consistent with results of Vermaet. al. [9] study in India which reported predominant male gender with AN in comparison to female. Our finding regarding gender is inconsistent with results of Kong et al [10] study in Mexico which found that AN prevalence among females is more than males. This inconsistency might be attributed to difference in prevalence of metabolic disorders among males and females. also to the small number of samples due to social causes regarding examination. Our study found a

significant association between AN lesions and public servants ( $p=0.02$ ).

Acanthosis nigricans patients in our study were commonly urban residents. Consistently, Dassanayakeet. al.[11] study in Sri Lanka stated that AN is highly predominant in urban areas with benefit of predicting the metabolic disorders.

In present study, the smoking history was present in 52% of AN patients. Wang et. al.[12] reported that smoking, obesity and alcohol consumption were found to be risk factors for development of acanthosis nigricans.

Measuring waist circumference and body mass index of AN patients in current study revealed that most of patients were overweight and obese. This finding is similar to results of many literatures like Karadağ et. al.[13] study in Turkey which reported that lifestyle changes leading to obesity is accompanied with high prevalence of acanthosis nigricans. About one third of AN patients had hypertension. Previous study carried out in UK found that AN is a significant predictor of hypertension in type 2 diabetic patients [14].

In present study, severe AN represented 42% of cases, while mild AN cases were 54% of cases and moderate cases were only 4% of them. This finding coincides with results of Patidar et al<sup>15</sup> study in India which found that severe acanthosis nigricans was present in about half of cases and severity of AN was significantly correlated to insulin resistance.

#### 5. Conclusions

The Acanthosis Nigricans is a common predictor for metabolic disorders like diabetes mellitus. Abnormal lipid profile is prevalent among patients with acanthosis nigricans. Glycated hemoglobin is more likely to be increased among patients with acanthosis nigricans. Acanthosis nigricans is more common in middle age, male obese urban resident patients with public servant occupation.

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