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ORIGINAL ARTICLE

# Evaluation of insulin resistance in obese women with and without acanthosis nigricans

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## ABSTRACT

Acanthosis nigricans is characterized by hyperpigmented velvety plaques of body folds and neck. Insulin could be a responsible factor in the pathogenesis of this condition and hyperinsulinemia: a consequence of insulin resistance stimulates the formation of these characteristic plaques. In this study, insulin resistance was compared in obese women with and without acanthosis nigricans. This was a cross-sectional study. Sixty-six obese women (32 patients with acanthosis nigricans and 34 patients without acanthosis nigricans) were selected randomly. Levels of fasting serum insulin and fasting blood glucose were measured in both groups and insulin resistance was determined using homeostasis model assessment. Glucose tolerance test also was performed for all of participants. Five (15.6%) patients with acanthosis nigricans and no (0%) patient without acanthosis nigricans had insulin resistance ($P < 0.05$). Six (18.7%) patients with acanthosis nigricans and one (2.9%) patient without acanthosis nigricans had impaired glucose tolerance test ($P < 0.05$). The mean levels of fasting serum insulin were 15.7 ± 8.7 and 12.2 ± 4.1 μm/mL ($P < 0.05$) and the mean values of insulin resistance index were 3.5 ± 1.9 and 2.6 ± 0.9 μm/mL between patients with and without acanthosis nigricans, respectively ($P < 0.05$). In Iranian obese women, acanthosis nigricans is a marker of insulin resistance.

**Key words:** acanthosis nigricans, insulin resistance, obesity.

## INTRODUCTION

Acanthosis nigricans is characterized by symmetrical, hyperpigmented, velvety plaques that may occur in almost any location and most commonly appears on the intertriginous areas of the axilla, groin and posterior neck.[1]

Acanthosis nigricans is assumed to be caused by factors that stimulate epidermal keratinocyte and dermal fibroblast proliferation. In the benign form of acanthosis nigricans, the factor is probably insulin and/or insulin-like growth factor that incites the epidermal cell propagation. In malignant acanthosis nigricans, the stimulating factor is hypothesized to be a substance secreted either by the tumor or in response to the tumor. Transforming growth factor-α, structurally similar to epidermal growth factor, is a possible candidate.[1,2] Hyperinsulinemia, a consequence of insulin resistance associated with obesity, stimulates the formation of characteristic plaques of acanthosis nigricans.[3] Insulin hormone binds to specific cell receptors and serves as a growth factor for keratinocytes and fibroblasts and therefore induces acanthosis nigricans lesions.[2]

Conflicting results have been reported about the true association between acanthosis nigricans and insulin resistance in past studies.[4,5] We designed the following study to evaluate this possible association in Iranian obese females.

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**Table 1.** Mean of anthropometric and some biochemical factors of obese women with and without acanthosis nigricans

| | Mean | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Group | Age (year) | Weight (kg) | Height (cm) | BMI (kg/m$^2$) | TG (mg/dL) | HDL (mg/dL) | LDL (mg/dL) | FBS (mg/dL) |
| With AN | 41 ± 13.6 | 81 ± 13 | 161 ± 10 | 31.4 ± 6 | 161 ± 98 | 40 ± 9 | 124 ± 37 | 89.5 ± 12 |
| Without AN | 36 ± 8.7 | 82 ± 17 | 163 ± 8 | 31 ± 5 | 157 ± 87 | 45 ± 13 | 177 ± 32 | 87.2 ± 8 |

AN, acanthosis nigricans; BMI, body mass index; FBS, fasting blood sugar; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides.

## METHODS

This was a cross-sectional study. Sixty-six obese women (32 patients with acanthosis nigricans and 34 patients without acanthosis nigricans) were selected randomly. All of the participants signed the consent form. Obesity was defined as a body mass index (BMI) of 30 or more.[6] The BMI was calculated by dividing bodyweight (kg) by the square of the height (m$^2$). Weight and height were measured while the subjects wore light clothing and were without shoes. Criteria used for the definition of insulin resistance were in accordance with the published guidelines proposed by the European Group of the Study of Insulin Resistance.[7] Fasting insulin × fasting blood glucose/22.5 was in accordance with the homeostasis model assessment of insulin resistance (HOMA-IR) calculated for each individual.[8]

Although the method to estimate insulin resistance is the hyperinsulinaemic euglycaemic clamp,[9] the HOMA-IR is strongly correlated with independent measures of insulin resistance using this method.[9] Subjects whose values exceeded the female-specific 75th percentile (i.e. 1.80 for women) were considered to have insulin resistance (HOMA-IR).[7] Oral glucose tolerance testing (OGTT) was performed with 75 g glucose p.o. and then serum glucose was measured after 30, 60 and 120 min. A glucose level after 2 h above 7.8 mmol/L (140 mg/dL) indicates impaired glucose tolerance.[10] Fasting serum insulin level was measured using the radioimmunoassay method and an INSIRMA kit (DRG Instruments GmbH, Marburg, Germany), and serum levels of fasting blood sugar (FBS), triglycerides (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were measured with the colorimetric method and compared between both groups. Hypertension was defined as a mean of at least two readings of 140 mmHg systolic blood pressure and/or 90 mmHg diastolic blood pressure or greater.[11] The exclusion criteria used were any systemic drugs in the past 2 months, pregnancy and history of diabetes mellitus (DM) or other metabolic disease. The collected data were analyzed using SPSS software ver. 13 (SPSS, Chicago, IL, USA). Comparison between proportions was performed using the $\chi^2$-test and the independent sample Student's *t*-test was used to compare between groups for quantitative variables.

## RESULTS

In total, 66 obese women, 32 with acanthosis nigricans (case group) and 34 without acanthosis nigricans (control group) were evaluated.

The mean of age, weight, height, BMI, serum TG, HDL, LDL and FBS are shown in Table 1. There were no significant differences in these parameters between the two groups ($P > 0.05$). Five (15.6%) patients with acanthosis nigricans and no (0%) patient without acanthosis nigricans had insulin resistance ($P < 0.05$). Six (18.7%) patients with acanthosis nigricans and one (2.9%) patient without acanthosis nigricans had impaired an glucose tolerance test ($P < 0.05$).

The means of fasting serum insulin were 15.7 ± 8.7 (Figure 1) and 12.2 ± 4.1 μm/mL in patients with acanthosis nigricans and patients without acanthosis nigricans, respectively ($P < 0.05$). The mean values of the HOMA-IR index were 3.5 ± 1.9 and 2.6 ± 0.9 μm/mL in patients with acanthosis nigricans and patients without acanthosis nigricans, respectively ($P < 0.05$). There was no significant difference in the values of TG, LDL, HDL and hypertension between two groups.

## DISCUSSION

In this study, we aimed at determining whether or not the presence of acanthosis nigricans in obese Iranian women can be a reliable cutaneous marker

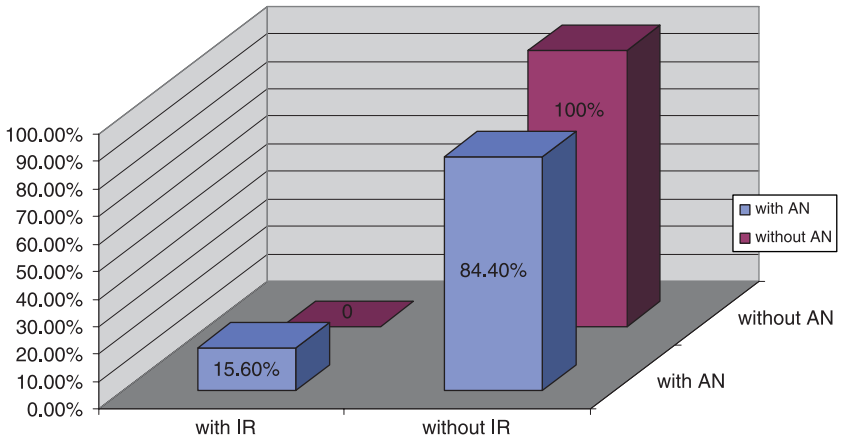


**Figure 1.** IR in groups with and without AN.

of insulin resistance. In order to obtain more accurate results, all of the evaluated cases and controls were matched for age, weight, height and BMI and only women with obesity were included. There was a significant difference between prevalence of insulin resistance between the cases and controls groups, and the mean of fasting serum insulin level and HOMA-IR index were significantly higher in patients with acanthosis nigricans. Acanthosis nigricans has been reported to be linked to hyperinsulinemia and obesity. A previous study has shown no significant difference in the prevalence of hyperglycemia and hyperinsulinemia between patients with and without acanthosis nigricans; however, levels of insulin increased progressively with obesity and acanthosis.[4]

In the another study of 184 females in the United Arab Emirates (UAE), patients with acanthosis nigricans had a higher prevalence of DM and insulin resistance as compared with those without acanthosis nigricans. Because insulin resistance was rather prevalent in the patients with acanthosis nigricans in the UAE, the authors suggested that identifying this skin lesion could help detect those subjects with a higher risk of DM and hormonal disturbances.[5]

In the study performed in Japanese children with acanthosis nigricans, significantly more glucose intolerance including impaired glucose tolerance and type Π diabetes was observed as compared with those children without acanthosis nigricans, and fasting plasma insulin concentrations were most significantly correlated with the presence of acanthosis nigricans. In addition, insulin resistance based on fasting plasma insulin concentrations was seen in significantly more children with acanthosis nigricans than in children without acanthosis nigricans, even in age- and percentage obesity-matched subjects with normal glucose tolerance during OGTT. The authors concluded that acanthosis nigricans could be a reliable cutaneous marker of insulin resistance in obese Japanese children.[12]

The results of the current study show that in Iranian female obese patients, acanthosis nigricans is a marker for insulin resistance. Screening the patients with acanthosis nigricans for hyperinsulinemia and insulin resistance has a major role in preventing the subsequent complications.

## REFERENCES

1 Schwartz RA. Acanthosis nigricans. *J Am Acad Dermatol*1994; **31**(1): 1–19.
2 Hermanns LE, Hermanns JF, Piérard GE. Juvenile acanthosis nigricans and insulin resistance. *Ped Dermatol* 2002; **19**(1): 12–14.
3 Davidson MB. Clinical implications of Insulin resistance syndromes. *Am J Med* 1995; **99**(4): 420–60.
4 Varthakavi P-K. A study of insulin resistance in subjects with acanthosis nigricans. *J Assoc Physicians-India* 2001 Jul; **49**: 705–712.
5 Lestringant G-G, Bener A. Association of Acanthosis nigricans with risk of diabetes mellitus and hormonal disturbances in females. *Int J Gynaecol Obstet* 2000 Dec; **71**(3): 267–9.
6 WHO. Report of a WHO Consultation on Obesity. Obesity – preventing and managing the global epidemic. *WHO/NUT/NCD* 1997.
7 Balkau B, Charles M. for the European Group for the Study of Insulin Resistance (EGIR). Comment on the provisional report from the WHO Consultation. *Diabet Med* 1999; **16**: 442–443.
8 Berglund G, Elmståhl S, Janzon L, Larsson SA. The Malmö Diet, Cancer Study. Design and feasibility. *J Intern Med* 1993; **233**: 45–51.

9 Raal FJ, Panz VR, Pilcher GJ, Joffe BI. Atherosclerosis seems not to be associated with hyperinsulinaemia in patients with familial hypercholesterolaemia. *J Int Med* 1999; **246**(1): 75–80.
10 Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 1997; **20**(7): 1183–1197.
11 Shrestha K, Singh DL, Bhattarai MD. The prevalence of hypertension and diabetes defined by fasting and 2-h plasma glucose criteria in urban *Nepal Diab Med* 2006); **23**(10): 1130–1135.
12 Yamazaki H, Sueshi I, Yoshida H. Acanthosis nigricans is a reliable cutaneous marker of insulin resistance in obese Japanese children *Ped Int* 2003; **45**(6): 701–705.