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Original Research Article

COMPARATIVE STUDY OF INSULIN RESISTANCE MARKERS IN PATIENTS WITH ACANTHOSIS NIGRICANS VERSUS OBESE CONTROLS

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ABSTRACT

Background: Acanthosis nigricans (AN) is a dermatological condition characterized by hyperpigmented, velvety thickening of the skin, frequently associated with underlying insulin resistance (IR). Obesity is an established risk factor for IR, but whether AN indicates a higher degree of metabolic derangement compared to obese individuals without AN remains to be clarified. This study aimed to compare insulin resistance markers between patients with AN and obese controls. **Materials and Methods:** A case–control study was conducted on 100 participants attending the dermatology and endocrinology outpatient clinics of a tertiary care hospital. Fifty patients with clinically diagnosed AN formed the case group, while 50 age- and BMI-matched obese individuals without AN served as controls. Fasting blood glucose (FBG), fasting insulin, and lipid profile were assessed. Insulin resistance was estimated using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). Statistical analysis was performed using independent t-tests and chi-square tests, with $p < 0.05$ considered significant. **Result:** The mean age of participants was 32.8 ± 8.6 years in the AN group and 31.9 ± 9.1 years in controls. Mean BMI was comparable between groups (31.2 ± 2.5 vs. 30.7 ± 2.8 kg/m², $p = 0.32$). The AN group demonstrated significantly higher fasting insulin levels (18.4 ± 5.9 µIU/mL vs. 12.6 ± 4.3 µIU/mL, $p < 0.001$) and HOMA-IR scores (4.12 ± 1.3 vs. 2.65 ± 1.1, $p < 0.001$). FBG was also elevated in the AN group (102.5 ± 11.8 mg/dL vs. 95.2 ± 10.6 mg/dL, $p = 0.01$). Lipid abnormalities were more frequent among AN patients, with higher triglyceride levels (168.7 ± 32.4 mg/dL vs. 145.1 ± 29.8 mg/dL, $p = 0.002$). **Conclusion:** Patients with acanthosis nigricans exhibit significantly higher levels of insulin resistance markers compared to obese controls, despite similar BMI. These findings suggest that AN may serve as an independent clinical marker of heightened metabolic risk and should prompt early screening and intervention strategies to prevent progression to type 2 diabetes mellitus.

INTRODUCTION

Acanthosis nigricans (AN) is a common dermatological condition characterized by hyperpigmented, velvety plaques most frequently involving the neck, axillae, and flexural surfaces. It is widely recognized as a cutaneous marker of underlying endocrine or metabolic disorders, particularly insulin resistance (IR) and hyperinsulinemia.[1] The prevalence of AN has been increasing in parallel with rising obesity rates worldwide, and its presence often precedes the onset of overt type 2 diabetes mellitus (T2DM).[2,3]

Insulin resistance plays a central role in the pathogenesis of both obesity-related metabolic syndrome and T2DM. Chronic hyperinsulinemia, a compensatory response to IR, is thought to stimulate keratinocyte and dermal fibroblast proliferation via insulin-like growth factor receptors, resulting in the characteristic skin changes seen in AN.[4,5] Therefore, AN is not merely a cosmetic concern but an important clinical indicator of metabolic dysregulation.[6]

Obesity, independent of AN, is also strongly linked with IR and cardiovascular risk. However, obese individuals with AN may have a greater degree of metabolic impairment compared to their obese counterparts without AN.[7,8] Previous studies have

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demonstrated that patients with AN exhibit higher fasting insulin levels and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) values than BMI-matched obese controls, suggesting that AN could serve as an independent marker for more severe IR.[9,10]

The present study was designed to compare insulin resistance markers—including fasting blood glucose, fasting insulin, and HOMA-IR—between patients with AN and obese controls without AN. This may provide evidence to establish AN as a clinical predictor of metabolic risk, facilitating early intervention strategies.

MATERIALS AND METHODS

Study Population: A total of 100 participants were included, divided into two groups:

- Cases (n = 50): Patients clinically diagnosed with acanthosis nigricans (AN) based on the presence of hyperpigmented, velvety skin changes on the neck and/or axilla.
- Controls (n = 50): Age- and body mass index (BMI)-matched obese individuals without clinical evidence of AN.

Inclusion Criteria

- Adults aged 18–50 years.
- BMI ≥ 30 kg/m².
- For cases: presence of AN confirmed by dermatological examination.
- For controls: obesity without any clinical sign of AN.

Exclusion Criteria

- Known cases of type 2 diabetes mellitus, polycystic ovarian syndrome, thyroid disorders, or Cushing's syndrome.
- Patients on medications known to affect insulin sensitivity (e.g., corticosteroids, metformin, thiazolidinediones).
- Pregnant or lactating women.

Clinical and Laboratory Assessment

Detailed demographic and anthropometric data including age, gender, weight, height, and BMI were recorded. For cases, the severity of AN was graded using Burke's quantitative scale.

Venous blood samples were collected after an overnight fast (8–12 hours). The following parameters were measured:

- Fasting blood glucose (FBG): by glucose oxidase-peroxidase method.
- Fasting serum insulin: by chemiluminescent immunoassay.
- Lipid profile: including total cholesterol, triglycerides, HDL-C, and LDL-C, using enzymatic methods.

Calculation of Insulin Resistance

Insulin resistance was assessed using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR).

Statistical Analysis

Data were analyzed using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as percentages. Independent t-tests were applied to compare mean values between cases and controls, while chi-square tests were used for categorical data. A p-value of < 0.05 was considered statistically significant.

RESULTS

A total of 100 participants were included, with 50 patients in the acanthosis nigricans (AN) group and 50 in the obese control group. The mean age was 32.8 ± 8.6 years in the AN group and 31.9 ± 9.1 years in controls, with no statistically significant difference (p = 0.64). Both groups were matched for BMI (31.2 ± 2.5 vs. 30.7 ± 2.8 kg/m², p = 0.32). Gender distribution was also comparable between the groups [Table 1].

Patients with AN exhibited significantly higher fasting blood glucose and fasting insulin levels compared to obese controls. The mean HOMA-IR score was also markedly higher in the AN group (4.12 ± 1.3 vs. 2.65 ± 1.1, p < 0.001). Lipid abnormalities were more frequent among AN patients, with significantly elevated triglycerides and lower HDL-C levels [Table 2].

Table 1: Baseline characteristics of study participants

Parameter	AN group (n = 50)	Obese controls (n = 50)	p value
Age (years)	32.8 ± 8.6	31.9 ± 9.1	0.64
Male (%)	28 (56%)	27 (54%)	0.84
Female (%)	22 (44%)	23 (46%)	
BMI (kg/m²)	31.2 ± 2.5	30.7 ± 2.8	0.32

Table 2: Comparison of biochemical parameters between AN patients and obese controls

Parameter	AN group (n = 50)	Obese controls (n = 50)	p value
Fasting blood glucose (mg/dL)	102.5 ± 11.8	95.2 ± 10.6	0.01
Fasting insulin (µIU/mL)	18.4 ± 5.9	12.6 ± 4.3	<0.001
HOMA-IR	4.12 ± 1.3	2.65 ± 1.1	<0.001
Total cholesterol (mg/dL)	196.8 ± 31.4	188.5 ± 28.9	0.18
Triglycerides (mg/dL)	168.7 ± 32.4	145.1 ± 29.8	0.002
HDL-C (mg/dL)	38.4 ± 6.2	44.1 ± 7.1	0.001
LDL-C (mg/dL)	122.7 ± 25.6	118.3 ± 24.2	0.41

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As shown in [Table 1], baseline characteristics such as age, sex distribution, and BMI were comparable between cases and controls, minimizing confounding effects. However, significant differences in insulin resistance markers were observed [Table 2]. Patients with AN had higher fasting insulin levels and HOMA-IR scores, indicating more severe insulin resistance compared to BMI-matched obese individuals.

DISCUSSION

The present study demonstrated that patients with acanthosis nigricans (AN) had significantly higher fasting insulin, HOMA-IR values, and dyslipidemia compared to obese controls matched for age and BMI. These findings highlight that AN is not merely a dermatological manifestation but a strong clinical indicator of underlying metabolic dysfunction.

Previous studies have established AN as a surrogate marker of insulin resistance (IR) and hyperinsulinemia.[1,2] The elevated fasting insulin levels observed in our AN group are consistent with reports from Stuart et al. and Hud et al., who described AN as a strong predictor of type 2 diabetes mellitus (T2DM), independent of BMI.[3,4] Our results also align with findings by Kong et al., who noted that children and adolescents with AN had higher HOMA-IR values compared to their obese peers without AN.[5]

In the present study, fasting glucose levels were significantly higher in the AN group, though still within the prediabetic range. This suggests that AN may serve as an early marker of glucose intolerance. Similar observations were made by Pollock et al., who reported impaired fasting glucose and hyperinsulinemia among adolescents with AN.[6] Furthermore, Hermanns-Lê and Piérard emphasized the mechanistic link between insulin-like growth factor receptor stimulation and keratinocyte proliferation, explaining the pathophysiological association between IR and AN.[7]

Lipid abnormalities were also more frequent in patients with AN, with higher triglycerides and lower HDL-C levels. This pattern is consistent with the metabolic syndrome profile described by Park et al.[8] Dyslipidemia in AN patients has been attributed to hepatic insulin resistance, which enhances lipogenesis and reduces lipoprotein clearance.[9] In our study, LDL cholesterol was not significantly different between groups, similar to findings by Burke et al.[10]

The higher degree of IR observed in AN patients suggests that AN may be a stronger predictor of cardiometabolic risk than obesity alone. Several investigators have emphasized the importance of dermatological markers in identifying individuals at high risk of T2DM and metabolic syndrome.[11,12] Sinha and Schwartz further proposed that AN can be considered a cutaneous phenotype of insulin resistance syndromes.[13]

From a public health perspective, the recognition of AN during routine dermatological or primary care visits could facilitate early metabolic screening and intervention. Misra and Khurana reported that South Asian populations are particularly vulnerable to insulin resistance at lower BMI thresholds, making clinical markers like AN highly relevant in these regions.[14] Similarly, data from the ICMR-INDIAB study demonstrated a rising burden of diabetes and prediabetes in India, underscoring the need for early identification of high-risk groups.[15]

Limitations of our study include the relatively small sample size and its single-center design, which may limit generalizability. Additionally, we did not assess dynamic insulin sensitivity measures such as the oral glucose tolerance test or euglycemic clamp. Nevertheless, HOMA-IR remains a validated and widely used surrogate for insulin resistance in clinical research.

CONCLUSION

In summary, this study supports the role of acanthosis nigricans as an independent marker of insulin resistance and dyslipidemia beyond obesity. Early identification of AN should prompt metabolic evaluation and targeted interventions to reduce long-term cardiometabolic complications.

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