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Original Research Article

Association between HOMA-IR and Treatment Response in Patients with Acanthosis Nigricans

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Abstract

Background: Acanthosis nigricans (AN) is a cutaneous marker frequently associated with insulin resistance (IR). The homeostasis model assessment of insulin resistance (HOMA-IR) is widely used to assess IR. Its association with treatment outcomes in AN is underexplored.

Objectives: To evaluate the relationship between baseline HOMA-IR and treatment response in AN, and to compare the efficacy of oral myo-inositol plus topical lactic acid (MYO+LA) with oral alpha-lipoic acid plus topical lactic acid (ALA+LA).

Methods: A hospital-based comparative study was conducted at a tertiary dermatology outpatient department between July 2022 and December 2023. Seventy-two patients with AN were alternately allocated to MYO+LA (n=36) or ALA+LA (n=36). Patients were followed for six months. Primary outcome was change in AN grade; secondary measures included HOMA-IR and correlation with clinical improvement. Statistical analysis was performed with ANOVA and correlation tests.

Results: Mean age was 31.47 years (range 20–55). Males constituted 70.83% and urban residents 80.55%. Neck was the commonest site (68.05%). Mean baseline HOMA-IR was 1.68. At six months, one-grade reduction was the most frequent response (42/72). Patients with lower baseline HOMA-IR had significantly greater improvement. The ALA+LA group showed a numerically higher mean grade reduction (+0.472 vs MYO+LA), but the difference was not statistically significant (p=0.53).

Conclusions: Lower baseline HOMA-IR values predict better clinical outcomes. Both regimens are effective, with no significant difference in efficacy. Early metabolic screening and individualized treatment improve outcomes.

Keywords: Acanthosis nigricans; HOMA-IR; insulin resistance; myo-inositol; alpha-lipoic acid; lactic acid; treatment response.

Introduction

Acanthosis nigricans (AN) is a dermatological condition characterized by symmetrical, velvety hyperpigmentation of the skin, predominantly affecting intertriginous sites such as the nape of the neck, axillae, and groin. Though primarily a cosmetic concern, AN often signals underlying systemic abnormalities, particularly insulin resistance (IR), and may rarely be a paraneoplastic marker of malignancy [1,2].

The prevalence of AN varies globally, influenced by ethnicity, obesity, and metabolic risk factors. In India, AN prevalence among obese individuals is reported as high as 86.6% [3], while in Brazil it is 76% [4]. IR is central to AN pathogenesis. Hyperinsulinemia stimulates keratinocyte and fibroblast proliferation via insulin-like growth factor (IGF-1) receptors, leading to epidermal thickening and hyperpigmentation [5]. HOMA-IR, introduced by Matthews et al. [6], is a validated surrogate marker for IR. While its role in metabolic syndromes is well documented, its predictive role for treatment response in AN remains unclear.

Therapeutic approaches include weight reduction, lifestyle modification, topical keratolytics, chemical peels, lasers, and systemic insulin sensitizers. Myo-inositol (MI), a naturally occurring polyol, improves insulin sensitivity, while alpha-lipoic acid (ALA), an antioxidant, enhances glucose uptake and reduces oxidative stress [7,8]. Topical lactic acid, an alpha-hydroxy acid, promotes keratolysis and improves texture. Few studies have directly compared MI and ALA in AN. This study aimed to assess the association of baseline HOMA-IR with treatment outcomes in

AN, and to compare MYO+LA versus ALA+LA regimens.

Materials and Methods

Study design and setting: A hospital-based comparative study conducted in the Skin & VD OPD of a tertiary care hospital, Jaipur, between July 2022 and December 2023.

Participants: Inclusion criteria included patients of all ages and both sexes with clinically diagnosed AN and informed consent. Exclusion criteria included refusal to participate.

Sample size and allocation: Seventy-two patients were enrolled. Odd-numbered patients received MYO+LA (n=36), even-numbered received ALA+LA (n=36).

Outcomes: Primary outcome was change in AN grading at six months. Grading system: Grade 1 (lesions on close observation), Grade 2 (limited to base of skull), Grade 3 (up to lateral neck margins), Grade 4 (severe, extending anteriorly). Secondary outcomes: baseline HOMA-IR, TG/HDL ratio, fasting/post-prandial insulin ratios.

Statistical Analysis: Data analyzed in Microsoft Excel. ANOVA compared treatment arms. Correlation coefficients assessed HOMA-IR and clinical outcomes. Significance was set at $p<0.05$.

Results

Baseline characteristics: Mean age 31.47 years (20–55); males 70.83% (51/72); females 29.17% (21/72). Urban residents constituted 80.55% (58/72). Neck was the commonest site (68.05%). Family history of diabetes was 19.44%. Mean baseline HOMA-IR: 1.68. Treatment groups were comparable at baseline. After six months, most patients had improvement. One-grade reduction was most frequent (42/72). Patients with lower HOMA-IR were more likely to respond with ≥1-grade reduction. ALA+LA arm showed numerically better outcomes but no significant difference ($F=0.40$, $p=0.53$). Correlation analysis showed HOMA-IR positively correlated with age ($r=0.31$).

Table 1: Baseline Characteristics of Study Population

Characteristic	Value
Mean Age (years)	31.47 (20–55)
Male sex	70.83% (51/72)
Urban residence	80.55% (58/72)
Family history of DM	19.44% (14/72)
Baseline HOMA-IR	1.68

Table 2: Treatment Response by HOMA-IR Categories

HOMA-IR	No reduction	1-grade	2-grade	3-grade
Low (<1.1)	29.4%	40.2%	30.4%	-
Medium (1.1–1.2)	20.6%	67.4%	12%	-
High (>1.2)	26.3%	60.1%	12.5%	1.1%

Table 3: Comparison of Treatment Arms

Outcome	MYO+LA	ALA+LA
Mean grade reduction	-	- (+0.472 higher than MYO+LA)
Proportion ≥1-grade reduction	Yes	Yes
ANOVA p-value	-	0.53 (NS)

Table 4: Correlation Analysis

Variable	Correlation coefficient (r)
HOMA-IR vs Age	0.31 (positive correlation)
HOMA-IR vs Grade reduction	Inverse correlation observed

Discussion

This study demonstrates that baseline HOMA-IR is a predictor of treatment response in AN. Lower HOMA-IR values correlated with higher probability of clinical improvement, while higher HOMA-IR was associated with reduced responsiveness. This supports the role of IR in AN pathogenesis [5,6]. Both MYO+LA and ALA+LA regimens were effective. ALA+LA showed numerically greater improvement, but without statistical significance. Thus, both regimens may be considered clinically equivalent [7–10].

Our findings align with earlier studies linking IR severity to AN severity and supporting insulin-sensitizing agents as therapeutic options [2,3]. Topical lactic acid, used in both arms, may have enhanced cutaneous response. Laser studies have also shown promise in resistant AN [6,8]. Strengths include systematic evaluation of HOMA-IR and treatment outcomes. Limitations include small

sample size, quasi-random allocation, single-center setting, and six-month follow-up. Larger randomized studies are warranted.

Overall, baseline HOMA-IR can guide prognosis and therapeutic expectations in AN.

Conclusion

Lower baseline HOMA-IR predicts better treatment outcomes in AN.

Both MYO+LA and ALA+LA are effective regimens with comparable efficacy. Individualized therapy considering metabolic risk factors is recommended.

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