



## ACANTHOSIS NIGRICANS - A PROSPECTIVE OBSERVATIONAL STUDY ON ALARMING INDICATOR FOR INSULIN RESISTANCE AND HYPERLIPIDAEMIA

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**ABSTRACT** Acanthosis Nigricans (AN) is characterized by dark, coarse, thickened skin with a velvety texture, being symmetrical distributed on the neck and flexures. This study aims to find the association of AN with serum fasting insulin levels (SFIL) and lipid profile in patients attending tertiary care hospital. 40 patients with AN attending DVL outpatient department were included in the study. Out of 40 patients, 29 were females (72.5%) and 11 were males (27.5%). Most common site involved was neck followed by flexures. 60% patients were overweight and 7.5% were morbidly obese (BMI >40kg/m<sup>2</sup>). 85% had deranged lipid profile, 72.5% had high SFIL. Out of 29 females, 8 (27.39%) had PCOD. Life style and behavioural modification have proven beneficial in the prevention of disorders associated with insulin resistance (IR) and individuals with AN must be targeted to prevent the serious consequences of IR.

**KEYWORDS :** Acanthosis nigricans, body mass index, serum fasting insulin level, hyperlipidemia

### INTRODUCTION:

Acanthosis nigricans (AN) is a common dermatological complaint seen in the Dermatology Outpatient department (OPD). AN is characterized by dark, coarse and thickened skin with a velvety texture, being symmetrically distributed on the neck, axilla, antecubital fossa and popliteal fossa, groin folds; histopathologically characterized by papillomatosis and hyperkeratosis of the skin<sup>1</sup>. AN is partially associated with obesity and insulin resistance, endocrinopathies, hyperlipidemia, drugs and estrogen<sup>2</sup>. Reports suggest it is a feature of metabolic syndrome (MS), hence early diagnosis of this condition with screening for MS is imperative<sup>3</sup>. Acanthosis nigricans may be benign and malignant<sup>4</sup>. Benign AN affects 20% of adults and 7% of children. Malignant acanthosis nigricans is rare<sup>5</sup>. AN is probably the most readily recognized skin manifestation of diabetes.

### Curth et al classified AN into 4 types.

1. Malignant AN (Type 1): It is a cutaneous paraneoplastic syndrome associated with adenocarcinoma.
2. True benign AN (Type 2): It is familial, present at birth or beginning of childhood.
3. Pseudo AN (Type 3): It is associated with several syndrome in which obesity, endocrinopathies and mainly insulin resistant state are the important component.
4. Drug induced AN (Type 4)<sup>1</sup>

Sinha and Schwartz classified AN as Obesity associated AN (Pseudo AN), Benign AN, Syndromic AN, Malignant AN, Unilateral AN, Acral AN, Drug induced AN, Mixed AN<sup>6</sup>

In hyperinsulinemia insulin directly effects on keratinocytes. Insulin augments androgen levels in women<sup>7</sup>. This study aims to investigate the clinic-demographic profile of patients with AN and to assess the correlation of AN with increased waist hip ratio (WHR), increased body mass index (BMI), type 2 diabetes mellitus, deranged lipid profile and hyperinsulinemia in patients attending tertiary care hospital.

### METHODOLOGY:

A single centre prospective study was conducted in DVL outpatient department in a tertiary care hospital, Kakinada from February 2019 to July 2019. Total study population is 40. Detailed history, clinical examination and relevant investigations including lipid profile and SFIL were obtained.

### Inclusion criteria:

All consenting patients and clinically suspected cases of acanthosis nigricans were included.

### Exclusion criteria:

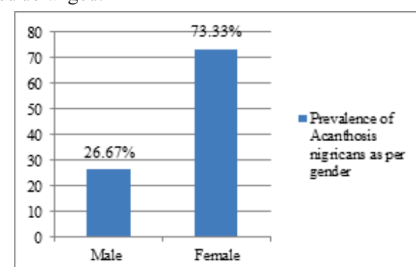
Pregnant mothers.  
Immunosuppressed patients  
Children <10 years  
Patients with malignancy

40 consecutive patients with AN were included. Detailed history including age, sex, occupation, symptoms, duration of lesion, associated skin conditions and comorbidities, family history of MS and AN. Menstrual and reproductive history was noted in females. Height, weight, Waist and Hip circumference were measured; BMI and WHR were calculated and categorized as per Asia Pacific guidelines. (Table 1)

**Table 1: Asia- Pacific guidelines for BMI and WHR<sup>7</sup>**

BMI	Weight (kg)/ height cm <sup>2</sup>	WHR
Normal	18-22.9 kg/m <sup>2</sup>	<0.8
Overweight	23-24.9 kg/m <sup>2</sup>	<0.81-0.85
Obese	25-29.9 kg/m <sup>2</sup>	<0.86-0.90
Morbid obese	>30kg/m <sup>2</sup>	>0.90

Thorough Cutaneous examination with AN lesions and associated lesions acrochordons, striae, Androgenetic Alopecia, acne etc were noted. Histopathological Examination done in consenting patients. Each patient was subjected to Fasting Blood sugar, Fasting lipid profile (TG and HDL) and fasting serum insulin level. Waist circumference (WC)  $\geq$  36 inches in males and  $\geq$  32 inches in female is considered abnormal and risky of developing metabolic syndrome. Fasting Blood Sugar : >100mg/dl was considered deranged. Fasting insulin level >80nIU/ml was considered deranged. Triglyceride > 150mg/dl and HDL < 40mg/dl in males and <50mg/dl in females was considered deranged.



**Figure 1: Prevalence of Acanthosis Nigricans as per gender**

### RESULTS:

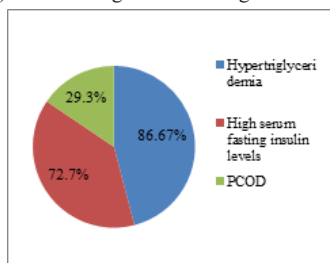
Out of 40 patients 29 were females (73.33%) and 11 were males (26.67%)(Figure 1).

70% had a sedentary and 30% had moderate workstyle. Most common site involved was neck (75%) followed by axilla (60%), groin (30%), face (15%) and inframammary regions (7.5%). Most common symptom was pigmentation (75%) followed by roughness (37.5%), dryness (22.5%) itching (15%) and bad odour (7.5%). 13.33% of AN patients had normal BMI, 53.35% belonging to grade 1 –overweight (23-24.9 kg/m<sup>2</sup>); 26.60% belonging to grade 2-Obese (25-29.9 kg/m<sup>2</sup>) 6.70% were morbidly obese with BMI >30 kg/m<sup>2</sup> as per asia pacific guidelines. Triglycerides were normal in 26 patients, borderline and high in 6 and 6 patients respectively and very high in 4 patients. (Table 2)

**Table 2: Distribution of AN patients with BMI and Triglyceride levels.**

BMI	Number(%)
Normal	5(13.35)
Overweight	21(53.35)
Obese	10(26.60)
Morbid obesity	4(6.70)
Triglycerides	
Normal (<150 mg/dl)	24(60)
Borderline high (150-199 mg/dl)	6(15)
High (200-499 mg/dl)	6(15)
Very high (>=500 mg/dl)	4(10)

Out of 40, 16 (40%) had deranged lipid profile. out of 29 females, 21 patients (72.42%) were with high serum fasting insulin level. out of 29 females, 8 (27.39%) were with PCOD. Out of 11 males, 8 males (72.72%) were with high serum fasting insulin level (Figure 2).



**Figure 2: Association of AN with other Co-morbidities**



**Figure 3 & 4: AN of neck & Closer view showing rough velvety textured skin**

#### DISCUSSION:

This study was carried out on an unselected population of patients with AN, who sought evaluation with the dermatologist for possibly cosmetic reasons and were diagnosed clinically and some confirmed with biopsy to have AN. There were more females than males (29 v/s 11; 73.33% v/s 26.67%). The overall prevalence of AN was higher in females possibly because it can be disfiguring and upsetting for the patients. The female preponderance in this study could be because obesity is another determinant of IR. In almost all populations, more women are obese and overweight than men<sup>9</sup>. Insulin clearly plays a central role in the presentation of AN. In states of insulin resistance and hyperinsulinemia, excess insulin binding to IGF1 receptor on keratinocytes and fibroblasts. IGF1 receptors are expressed on basal keratinocytes and are upregulated in proliferative conditions. Thus high insulin stimulates fibroblast proliferation through IGF1 receptors. The above changes of both fibroblasts and keratinocytes leads to phenotypic AN<sup>9</sup>. In our study hyperinsulinemia is associated with AN. 85% of patients in our study were with hyperlipidemia which indicates its close association with AN. Consistent with Mishra et al., increased WHR, hyperglycemia, dyslipidemia and hypertension were higher in our patients with AN<sup>10</sup>. Neck was the most common site involved and

pigmentation was the most common symptom which is in concordance with the study done by Nithun et al and Varthakavi et al<sup>10,11</sup>. No patient in this population manifested either generalized hyperpigmentation or mucosal involvement. It commonly involves the flexural areas, particularly the axillae, inguinal region, inframammary region and neck. In its most developed form, AN could involve almost the entire body, especially when it is a manifestation of internal malignancy especially the GI tract.

AN could occur - (a) as genito - developmental or nevoid (b) due to friction and maceration as in obesity (c) epidermotrophic as in acromegaly and these factors could affect the area of distribution<sup>12</sup>. Actually, today it is being recognized that IR, whatever its cause, stimulates insulin secretion and that the increased insulin levels stimulate IGF-1 receptors on various tissues. In the skin, stimulation of the IGF - 1 receptors on keratinocytes leads to excessive epidermal growth. Hence AN is considered as an epiphenomenon of the IR state. As it is evident from our study, AN is a marker for insulin resistance. Obese acanthotics may be more severely IR than their non-acanthotic counterparts. Also, it is a rare condition, not every obese individual manifests AN. Acanthosis occurs in patients with hyperinsulinemia owing to stimulation of the insulin like growth factor - I and epidermal growth factor, which cause proliferation of the epidermal cells.<sup>12</sup>

Life style and behavioural modification have proven beneficial in the prevention of several disorders associated with insulin resistance. Perhaps individuals with AN are another cohort that must be targeted for lifestyle modification, so that the serious consequences of IR may be avoided.

#### CONCLUSION:

Though patients with AN attend hospital for cosmetic concern, it is a predictor of underlying insulin resistance and hyperlipidemia. Female obese patients preponderance was seen in our study. Hence SFIL and lipid profile screening is mandatory for all obese patients with AN, for early intervention of underlying metabolic disorders and to avoid risk of cardiovascular complications.

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