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A clinico-epidemiological study of patients with acanthosis nigricans

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Abstract:
Background: *Acanthosis Nigricans (AN) is characterized by thickened, hyperpigmented plaques with a velvety texture. The lesions are symmetrically distributed on the flexural areas which include posterior neck , axillae, antecubital fossa and other intertriginous areas. Different varieties of acanthosis nigricans include benign, obesity associated, syndromic, malignant, acral, unilateral, drug-induced and mixed type.*
Aim: *To study the clinico-epidemiological features of patients with acanthosis nigricans.*
Materials and Methods: *An observational, descriptive, institution based cross sectional study of 18 months duration conducted at the out-patient department of Dermatology,Venereology and Leprosy of National Institute of Medical Sciences and Research, Jaipur, Rajasthan in patients of all ages and sex presenting with acanthosis nigricans (AN).*
Results: *A total of 104 patients of acanthosis nigricans fulfilling the inclusion criteria were included in the study.Out of total patients, 64 were females and 40 were males.The most common age group was between 21 to 40 years in 68(65.38%) patients.The mean age in the study was 35.05 years.The most common area involved was the neck in all patients. The associated dermatological diseases were hirsutism (28.85%), acne vulgaris(26.92%), dermatoses papulosa nigra(20.19%), skin tags (18.27%) and alopecia (5.77%).The other co-morbidities associated with AN were (29.81%) diabetes mellitus, (17.31%) thyroid disorder (hypothyroidism). The association of AN with obesity was seen in 30.76% of patients and PCOD in 20.31% patients. Family history of AN was present in 62 (59.61%) patients.*
Conclusion: *AN was more common in female patients than male and more in urban areas which may be related to high calorie intake, sedentary life style, obesity, high BMI and dyslipidemia in these areas.*
Keywords: *Acanthosis nigricans, Insulin resistance, Obesity*

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I. Introduction

Acanthosis Nigricans (AN) is characterized by thickened, hyperpigmented plaques with a velvety texture.The lesions are symmetrically distributed on the flexural areas including posterior neck , axillae, antecubital fossa and other intertriginous areas. At times may also affect eyelids, lips, vulva, mucosal surfaces, dorsal hands, and flexural areas in the groin, knees and elbows(1). Women may also develop lesions on the nipple. The most common site of acanthosis nigricans in the children is posterior neck. Occasionally, the lesions may become generalized and involve mucosa(2).

Acanthosis nigricans is typically asymptomatic, but sometimes can be pruritic. There are different varieties of acanthosis nigricans which include benign, obesity associated, syndromic, malignant, acral, unilateral, drug-induced and mixed type(3).

Acanthosis nigricans is common in obese adolescents. The prevalence in general population is exactly unknown. It has been increasing recently due to the rising prevalence of obesity and diabetes mellitus. It ranges from 7% to 74% with significant female predominance its prevalence varies among different races(4).

The severity of acanthosis nigricans increases with increasing BMI, waist-hip ratio, body fat percentage and diabetes mellitus(5).

The onset is insidious. Lesions of acanthosis nigricans may be present at any age, including at birth, although it is present more commonly in adulthood. Malignant acanthosis nigricans occurs more frequently in elder age group(6).

It frequently goes unnoticed or simply mistaken as dirt by the patient and the family[7,8,9]. The involved skin appears light brown to black in color, depending on the patient's skin complexion. It is poorly marginated with accentuation of skin markings giving rise to a roughened, velvety texture. As the lesion progresses, it may become papillomatous or verrucous plaque[10,11]. Mucosal involvement is rare in obesity associated AN but commonly seen in malignancy associated cases[3]. Clinicians should recognize acanthosis nigricans as it heralds various disorders ranging from endocrinological disturbances to malignancy[12]. Early recognition of these conditions is helpful in early diagnosis of underlying disease and appropriate treatment.

Diagnosis of acanthosis nigricans is largely clinical with histopathology needed only for confirmation. Acanthosis nigricans is a marker for disorders of insulin resistance, endocrine abnormalities, internal malignancy ,gonadal disease and various other disorders.

Early recognition of the underlying conditions is essential for prevention of disease progression[13] and timely treatment.

Considering these aspects, this study was undertaken to find out the clinical features, its association and epidemiological aspects of acanthosis nigricans.

There are many reports of innumerable dermatological entities presenting with acanthosis nigricans. But, very limited studies have been conducted on the clinico-epidemiological features of patients with acanthosis nigricans. Therefore, this study was taken up to work upon.

II. Materials and Methods

Study design: It was an observational, descriptive, institution based cross sectional study carried out to study the clinico-epidemiological features of patients with acanthosis nigricans.

Study location: The study was conducted at the out-patient department of Dermatology,Venereology and Leprosy of National Institute of Medical Sciences and Research, Jaipur, Rajasthan.

Study population: All the patients presenting with acanthosis nigricans as per inclusion criteria were recruited in the study.

Study duration: The study was done over a period of 18 months .

Sample size:104 patients.

Sample size calculation:

Sample size was calculated using the formula,

$n=4pq/e^2$

p=93%

q=100-p

n=4*93*(100-93)/52

n=104

Where 'n' is desired sample size, 'p' is prevalence , 'q' is quotient and 'e' is margin for error. The study included 104 patients as final valuable subjects assuming that neck involvement was observed in 93% cases of acanthosis nigricans associated with Metabolic syndrome.

Selection criteria of patients

Inclusion criteria:

1. Patients of all ages and sex presenting with acanthosis nigricans willing to participate in the study were included.

Exclusion criteria :

1. Unwilling patients were excluded from the study.

III. Observations and Results

In this study the following observations were made :

Total number of patients of acanthosis nigricans studied during the period was 104.

Age distribution

In the present study, the patents were upto 60 years; the mean age being 35.05+-9.51 years. The youngest patient who presented with acanthosis nigricans was 14 years old and the eldest was 58 years old. Majority of the patients were in the age group 21 to 40 years. Only 11 (10.58%) cases were above 40 years of age.(TABLE 1)

Table 1 : Age distribution of patients of AN (n= 104)

Age group	Number of patients	Percentage
Upto 20 years	25	24.04%
21 to 40 years	68	65.38%
41 to 60 years	11	10.58%

Sex distribution
A female preponderance was seen in the study with a female to male ratio of 1.6:1(TABLE 2)

Table 2 : Sex distribution of patients in the study population

Sex	Number of patient	Percentage
Female	64	61.54%
Male	40	38.46%

Distribution of sites affected with AN
Out of total 104 patients neck only was involved in 67(64.42%) patients. The neck and axilla were involved in 21 (20.19%) patients. Dorsum of the fingers and toes along with neck were affected in 10 (9.62%) patients.The neck, axilla and antecubital fossa (AC Fossa) were affected in 06 (5.77%) patients. (Table 3)

Table 3 : Distribution of sites affected with AN (total= 100)

Site	Total number of patients	Percentage
Neck	67	64.42%
Neck+Axilla	21	20.19%
Neck+Acral parts	10	9.62%
Neck+Axilla+AC fossa	06	5.77%

Figure 1a showing AN over neck , 1b showing AN over axilla and 1c showing AN over popliteal fossa

1a 1b 1c

Co-morbidities of patients with AN
Among the total 104 cases affected with AN, 30 (28.85%) patients (females) had hirsutism, 28(26.92) patients had acne vulgaris,21 (20.19%) patients had dermatoses papulosa nigra (DPN) ,19 (18.27) patients had skin tags and 06(5.77%) had alopecia. (Table 4)

Table 4 : Proportion of cases of AN associated with other skin diseases

Name of other diseases	Male	Female	Total number of patients	Percentage
Hirsutism	00	30	30	28.85%
Acne	13	15	28	26.92%
DPN	12	09	21	20.19%
Skin tag	08	11	19	18.27%
Alopecia	04	02	06	5.77%

Etiological association
Out of total 104 patients of AN, 31 (29.81%) patients had diabetes mellitus, majority of whom had type-2 DM and 18(17.30%) patients had associated thyroid disorder (hypothyroidism). Total cholesterol level was above 200 mg/dl in 15 (14.42%) of these patients. 32(30.77%) patients had hypertriglyceridemia and obesity was present in 34 (32.69%) patients of AN. (TABLE 5)

Table 5 : Proportion of cases of AN showing etiological association with other diseases

Name of other diseases	Number of patient	Percentage
Obesity	34	32.69%
Hypertriglyceridemia	32	30.76%
Diabetes Mellitus	31	29.81%
Hypothyroidism	18	17.31%
Hypercholesterolemia	15	14.42%

Family history of AN:
Family history of AN was present in 62(59.61%) patients out of 104 .
Body mass index (BMI) distribution:
Body Mass Index was calculated by using the formula weight in kilograms/height in meter square. (Table 6)

Table 6 : Distribution of body mass index

BMI in kg/m^2	Male	Female	Total
<20	6	3	9
20-24.99	7	13	20
25-29.99	13	28	41
>= 30	14	20	34
Total	40	64	104

In our study, 41(39.42%) patients were overweight (25-29.99) and 34(32.69%) were obese (>30).

Ultrasound abdomen
The ultrasound abdomen was done in all female patients.Out of 64 females, 13 (20.31%) had associated polycystic ovarian disease (PCOD).(Table 7)

Table 7 : Ultrasound abdomen report

	Normal	PCOD	Total no. of female
Female	51	13	64

IV. Discussion

The present study included 104 patients of AN. These were examined, findings were recorded on proforma and analysed.

Acanthosis nigricans is a common dermatologic condition involving posterior neck, axilla, elbows and knees, with the neck being involved in all the patients(1,2).

Age distribution: In this study the most common age group observed was between 21 to 40 years that is 68(65.38%) patients out of 104. The number of patients in extremes of age group was low (24.04% upto 20 years of age and 10.58% in age group 41 to 60 years).
The mean age in our study was 35.05 years.

Sex distribution: In our study, the number of female patients with acanthosis nigricans outnumbered males with 64 females and 40 males and the ratio of female to male patient was 1.6:1.
The higher prevalence of AN in the female population may be due to the fact that the females had relatively higher BMI, higher calorie intake and more sedentary work.

Site distribution of the lesions: The present study showed that out of total 104 patients, the neck was involved in all the patients.The neck and axilla was involved in 20.19% of the patients. The neck,axilla and antecubital fossa were simultaneously affected in 5.77% patients. Dorsa of the fingers and toes along with neck were affected in 9.62% patients.

Associated dermatological diseases: In the study of 104 patients affected with AN, hirsutism was present in 28.85% patients, acne vulgaris in 26.92% patients, dermatoses papulosa nigra(DPN) in 20.19% patients, skin tags in 18.27% patients and alopecia in 5.77% patients.

Co-morbidities : In the study, out of total 104 patients of AN, 29.81% patients had diabetes mellitus, 17.31% had thyroid disorder(hypothyroidism) which is in concurrence with various other studies. Obesity was associated with AN in 30.76% of patients.

Body mass index (BMI) : In the study, 72.11% patients were obese,out of which 39.42% patients were overweight and 32.69% patients had obesity with a BMI more than or equal to 25.There appears to be a positive correlation of extent of AN with increasing anthropometric measurements.

Polycystic ovarian disease: In the study, ultrasound screening of female patients showed PCOD in 20.31% patients with acanthosis nigricans(AN). Family history of AN was present in 62 (59.61%) patients. However we could not find any patient of AN associated with malignancy.This was in concurrence with the various other studies (Grandhe et al [(14)], Hoffmann et al [(15)]) which also did not find any underlying malignancy.

V. Conclusion

The study concluded that AN is more in female patients than male and more so in urban areas which may be related to high calorie intake and sedentary life style in these areas.AN may start simultaneously at multiple areas of the body.

There was a significant association between AN and anthropometric measurements like height, weight and waist-hip ratio. Association of obesity, high BMI and dyslipidemia strengthen the role of high calorie intake and sedentary life style.

Prevalence of AN was positively correlated with severity of obesity and diabetes mellitus. Hence, AN can be used as a reliable cutaneous marker for early detection of people who are at greater risk of having metabolic syndrome and various other endocrine disorders.At the same time, patients with AN can be targeted for lifestyle and behavioural modifications as well as treatment at an early stage to avoid the serious consequences of metabolic syndrome, endocrine disorders and even malignancy at times.

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