Original Research Article

Prevalence of Acanthosis Nigricans in a Population Attending a Tertiary Care Centre in Western India and it's Utility to Detect Metabolic Syndrome

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Abstract

Background: Acanthosis Nigricans (AN) is a dermatosis with thickened, hyperpigmented plaques immediately recognizable. The metabolic syndrome (MetS) is a collection of metabolic risk factors that include central obesity, glucose intolerance, hyperinsulinemia, low HDL cholesterol, high triglycerides, and high blood pressure. The skin biomarker AN is linked to this syndrome.**Aims and Objectives:** To study the prevalence of AN and associated factors in patients that predicts the risk of MetS.**Materials and Methods:** Five hundred and forty-seven patients with AN were studied over a period of two years. Complete dermatological assessment of skin, including distribution and grading of AN, was performed. Evaluation for metabolic syndrome, including body mass index (BMI), waist and hip circumference, waist-hip ratio (WHR), blood pressure, was noted. Laboratory investigations like fasting blood sugar (FBS), post prandial blood sugar (PPBS), fasting insulin, lipid profile, serum B12, and thyroid function test were done in all patients of AN. **Results:** Prevalence of AN was 6.5%. The majority had an age between 11-20 years (32.9%). Benign acquired AN (70.7%) was the commonest type of AN, while syndromic AN (17.9%) was the second most common type. Patients of AN with MetS were older (28.4±11.7 years; p=0.0184), had BMI more than 30 (31.5±4.6; P<0.001), higher waist circumference (100.6±10.9 cm; P<0.001), higher WHR (0.92±0.05; P=0.0242), higher FBS (102.3±21.6; P<0.001) and PPBS (130.9±39.1; P<0.001) and higher fasting insulin level (25.7±13.7; P<0.001) compared to those without MetS. Linear regression revealed that BMI (R2=0.08334, P=0.0004 for patients of AN without MetS and R2=0.06377, P<0.001 for patients of AN with MetS), waist circumference (R2=0.05999, P=0.003 for patients of AN without MetS and R2=0.07336, P<0.001 for patients of AN with MetS) and WHR (R2=0.03603, P=0.0222 for patients of AN without MetS and R2=0.008235, P=0.0764 for patients of AN with MetS) has a much more significant effect on insulin in the patients of AN with MetS.**Conclusion:** AN was common in our study population and the presence of AN strongly predicts metabolic syndrome.

Keywords: metabolic syndrome, Acanthosis Nigricans, body mass index, insulin.

Introduction

Acanthosis Nigricans (AN) is a skin disorder characterized by hyperpigmentation and hyperkeratosis, occurring mainly in the neck, axilla, and groin.[1] Other sites such as antecubital and popliteal fossae, umbilicus, and perianal areas can also be involved. Involvement of the dorsum of the hands and fingers can occur in patients with advanced AN. Diffuse palmoplantar hyperkeratosis may be seen. [2]

Acanthosis Nigricans has been classified into the following types: hereditary, benign, pseudoacanthosis nigricans, drug-induced, malignant and nevoid. Common associated endocrine disorders are hypothyroidism, insulin-resistant diabetes mellitus, acromegaly, Cushing"s disease, and acral hypertrophy syndrome. [3]

Acanthosis Nigricans is more commonly associated with endocrinologic abnormalities, particularly insulin resistance (IR). Such patients are typically overweight, and the onset of the condition is usually insidious[4].The metabolic syndrome (MetS) is a cluster of obesity, low HDL cholesterol, hypertension, impaired fasting glucose, and elevated triglycerides, reflecting underlying insulin resistance. MetS and insulin resistance are risk factors for type 2 diabetes and are associated with cardiovascular disease morbidity and mortality. [5] Insulin resistance and related metabolic conditions are becoming increasingly frequent, and a substantial proportion of apparently healthy people are reported to be insulin resistant. [6]

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There is limited data available on the prevalence of AN in western India. Studies addressing the associated factors in AN patients for predicting the risk of MetS are inadequate. Hence this study was conducted to determine the prevalence of AN and it's utility to detect the MetS.

Materials and Methods

In the present observational cross-sectional study, 103853 patients visited Skin Outpatients Department (OPD) of our hospital from September 2013 to August 2015. Patients of AN of all the age groups attending the OPD and those referred from other departments were included. The ethical clearance was given by the Institutional committee as per ref. No. EC/certi/84/15. Patients not willing to give consent for study/photography were excluded.

Based on a thorough history, examination, and relevant investigations, a diagnosis of AN was made. Informed written consent for the use of medical records and taking photographs was obtained from every patient. Confidentiality of all records was maintained.

A detailed history regarding the age, gender, religion, occupation, family history, personal history, and treatment history, menstrual and obstetric history was taken.

Complete dermatological assessment of skin including distribution and grading of Acanthosis nigricans was done. Any involvement of hair and mucosa was also noted. Comprehensive general and systemic examinations were done. Evaluation for metabolic syndrome [body mass index (BMI), waist and hip circumference, waist-hip ratio (WHR), blood pressure] was done.

Laboratory investigations like fasting blood sugar (FBS), post prandial blood sugar (PPBS), fasting insulin, lipid profile, serum B12,

and thyroid function test were done in all patients of AN. Other investigations such as postprandial insulin, hormonal profile, complete hemogram, liver and renal function tests were done in a few of the patients of AN. Ultrasonography of the Abdomen, kidneys, ureter and bladder and pelvis was done whenever required. Punch biopsy was taken from the lesions in a few of the patients of AN. Patients were counselled adequately for lifestyle modification, and appropriate referrals were made.

Data were evaluated by Graphpad software. As all parameters showed normal distribution, parametric tests were used in statistical evaluation. Descriptive data were expressed as mean and standard deviations. The results were analyzed by Student's t-test, χ2-test, and Z test. Statistical significance was set as $P < 0.05$.

Results

Of the 103853 patients that attended the skin OPD during the study period, 670 patients were diagnosed as AN based on clinical evaluation. Thus, the overall prevalence of AN in our hospital-based cross-sectional study for two years is 6.5 per 1000 population.

Out of the 670 patients counselled for lifestyle modification and asked for a detailed workup of AN, 547 patients agreed to the workup. Thus, our study group constituted 0.53% of the total OPD load.

The commonest age group with AN was 11-20 years with 32.9% patients, 24.9% patients were between 21- 30 years, 24.5% patients were between 31-40 years, 8.6% patients were between 41-50 years, 5.5% patients were less than 10 years of age, and 3.7% patients were more than 50 years of age. The youngest and eldest age of presentation of AN was 5 years and 71 years, respectively.

Most of the patients of AN were students (51%), 153(28%) were housewives, and the rest of the patients of AN were laborers, drivers, businessmen, teachers, government employees, and retired persons. A family history of AN was present in 279 (51%) of the patients.

Out of the 547 patients of AN examined, 296(54.1%) patients were affected with AN involving the flexures, 138(25.2%) patients had generalized involvement with AN. The face was affected in 130(23.8%) patients; 20(3.7%) patients had AN involving only the extensors, while palms and oral mucosa were engaged in two and one patient of malignant AN, respectively.

Most common associated dermatological conditions in the patients of AN was acrochordons [191 (34.9%)], alopecia [139 (25.4%)], acne [132 (24.1%) and hirsutism [57 (19.4%)].

Of the adult patients of AN, 163(40.2%) belonged to obesity class I, 61(15.1%), and 16(4%) patients belonged to obesity class II and III, respectively. The mean BMI of adult males and females was 30.1 and 31.4, respectively. In children and adolescents, obesity was diagnosed based on BMI for age charts of WHO and IAP. Of the 142 children and adolescents, obesity was diagnosed in 95(66.9%) patients of AN. The mean BMI of males and females was 24.7 and 26.3, respectively.

Of the 294 females of the reproductive age group, menstrual disorders were found in 77 (26.2%) patients, and 18(6.1%) female patients gave a history of amenorrhoea. PCOS was diagnosed in 73 (24.8%) patients of the reproductive age group.

Table 1: Associated abnormality present in patients with acanthosis nigricans

Associated abnormality		Number of patients (%)
Hypertension		61 (11.2)
Diabetes Mellitus		102 (18.6)
Hyperinsulinemia		241 (44.1)
Dyslipidaemia	Raised TG	109 (19.9)
	Low HDL	126 (23)
B12 deficiency		213 (38.9)
Thyroid dysfunction		22 (4)

Data is expressed as number of patients (percentage). TG: triglyceride; HDL: high density lipoprotein

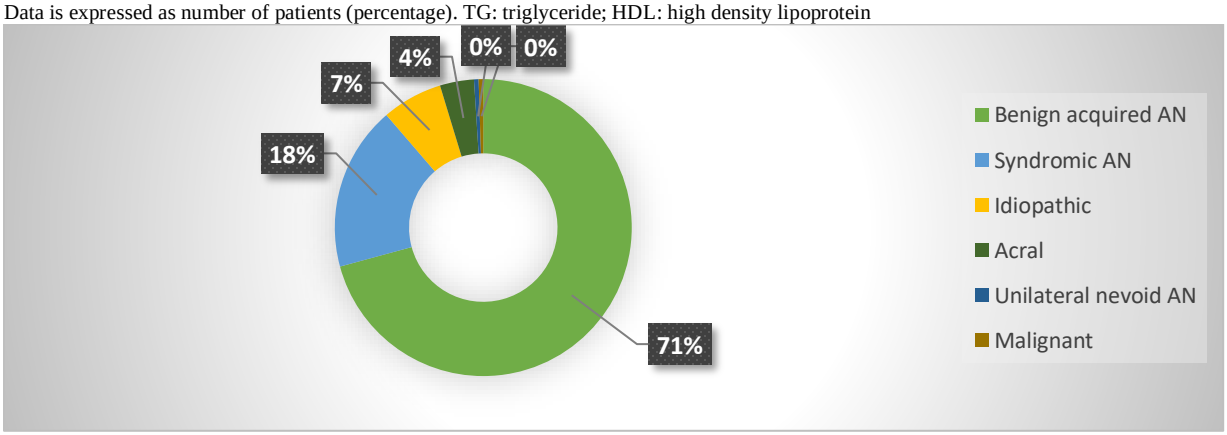

Fig. 1: Types of acanthoses nigricans in-study population

Metabolic syndrome (MetS) was diagnosed in 387 (70.7%) patients of acanthosis nigricans based on NCEP- ATP III criteria. The IDF criteria for diagnosing MetS in children cannot be interpreted in children < 10 years. The present study comprises 15 patients of < 10 years. Thus, MS could not be diagnosed in these 15 patients of AN.

Table 2: Demographic, anthropometric, and investigational variables of AN subjects with and without MetS

Variable	AN with MetS (n=387)	AN without MetS (n=145)	P-value
Age	28.4±11.7	25.7±11.8	0.0184
BMI	31.5±4.6	25.3±4.6	<0.001
Waist circumference	100.6±10.9	88.4±8.8	<0.001
WHR	0.92±0.05	0.91±0.03	0.0242
FBS	102.3±21.6	93±12.2	<0.001
PPBS	130.9±39.1	115±22.6	<0.001
Fasting Insulin	25.7±13.7	18.5±7.5	<0.001

Data are expressed as mean ± standard deviation. BMI: body mass index; WHR: waist to hip ratio; PBS: fasting blood sugar; PPBS: postprandial blood sugar; AN: acanthosis nigricans; MetS: metabolic syndrome. P value of <0.05 is considered as significant.

Linear regression revealed that BMI (R2=0.08334, P=0.0004 for patients of AN without MetS and R2=0.06377, P<0.001 for patients of AN with MetS), waist circumference (R2=0.05999, P=0.003 for patients of AN without MetS and R2=0.07336, P<0.001 for patients of AN with MetS) and WHR (R2=0.03603, P=0.0222 for patients of AN without MetS and R2=0.008235, P=0.0764 for patients of AN with MetS) has a much more significant effect on insulin in the patients of AN with MetS.

Discussion

The overall prevalence of AN in our hospital-based cross-sectional study during two years is 6.5 per 1000 population. After a thorough literature review, we could not find a comparative study that measured the prevalence of AN and MetS in any hospital set up in India. But there is a study done in 2011 by Dassanayake et al. who observed the prevalence of AN and MetS in the community in Sri Lanka as 17.4% and 34.8%, respectively. [2] The reported prevalence has significantly varied in different studies, from 0.5% in white children [7] to 74% in obese adults [8]. Much of this variability may be attributable to nonstandardized methods.

The age profile of our patients ranged from 5 to 71 years, with most patients being from the 11-20 age group. This study is comparable to the study done by Puri et al., where the maximum number of patients of AN were of the same age group.[9]

Females were more conscious about AN, with a ratio of male to a female being 1:2.04. This study is comparable to the study done by Puri et al. 23, where the ratio was 2:3. [9] That is probably due to decreased importance given by men to cosmesis.

In our study, most of the patients of AN were students and housewives. One reason may be increased cosmetic consciousness in them. Also, it might be an alarm regarding their unhealthy sedentary lifestyle.Almost half of the patients of AN gave a family history of DM, HT, obesity, CVD, thyroid dysfunction, or MetS. This follows the thrifty genotype-phenotype hypothesis[10].In most of the patients of AN, flexures were commonly involved, followed by the generalized AN - both flexures and extensors. Puri et al. also found similar results. [9] However, one significant observation in our study was the facial involvement (including periorbital hyperpigmentation) in 23.8% of AN patients. Thus, metabolic melanoses should be kept in mind every time while seeing any patient with facial hypomelanosis.

Acrochordons were found in 34.9% of patients of AN. This is in comparison to the study by Banik et al.24.1% of the AN patients had concomitant Acne vulgaris. [11] This is in contrast to the survey by Kubba et al. [12]

The average BMI of adult patients of our study was high (30.1 in males and 31.4 in females). This is in contrast to the study done by Patidar et al., where males' and females' mean BMI was 25.7 and 29.2, respectively. 40.2, 15.1, and 4% adult patients of AN belonged to Obesity Class I, II, and III, respectively. [13] Similar results were observed in the study done by Puri et al., wherein children and adolescents, obesity was diagnosed in 66.9% of patients of AN. [9]

Of the 294 females of the reproductive age group, 26.2% and 6.1% gave a history of menstrual disorders and amenorrhoea. PCOS was diagnosed based on history, examination, biochemical and radiological evidence in 24.8% of females. Hypertension was seen in 11.2% of patients of AN. Diabetes Mellitus and Hyperinsulinemia were seen in 18.6 and 44.1%, respectively. Puri et al. made similar observations in their study. [9]

Lower Serum B12 levels were observed in 38.9% of patients of AN. Contrary to our study, Mahajan et al.109 observed 25% of patients of suspected deficiency as B12 deficient. A large number of our patients were vegans. This very well explains our observation of more B12 deficient patients. Thyroid abnormalities were seen in 4% of patients of AN.

In our study, the most common type of AN was the obesity-associated AN found in 70.7% of the patients. The second most common was syndromic AN (including HAIR-AN & autoimmune) found in 17.9% of patients. Acral variety of AN was found in 3.7%. The least common were the nevoid and malignant AN seen in 0.5% each. Similar results were seen in the study by Puri et al.23. In 6.6% of patients of AN, no underlying etiology was found[9].Of the 532 patients of AN with or without MetS, 387(70.7%) patients were found to have MetS. This is a very significant observation (p<0.0001) in comparison to the community prevalence of AN with MetS in the study by Dassanayenke et al. [2]

There was a significant statistical difference (p <0.05) between the two groups regarding all the variables such as age, BMI, waist circumference, WHR, FBS, PPBS, and fasting insulin. Similar observations were made by Dassanayenke et al. [2]

On analysis of the two groups (AN with and without MetS) by linear regression, we found a positive correlation between BMI (p<0.0001), Waist circumference (p<0.0001), and WHR with the fasting insulin values. This suggested the significance of anthropometry and laboratory evaluation of fasting insulin in patients of AN. Similar observations were made in the study done by Bonet et al. [14] and Varthakavi et al [15].

Conclusion

The prevalence of AN in our hospital during the study period of two years is 6.5 per 1000 population. AN is more prevalent in young females, students, and homemakers. Family history of AN can be a contributing factor in developing AN. Patients with AN have high BMI. Lower serum B12 levels are more prevalent in AN patient. The most common type of AN was the obesity-associated and syndromic AN (including HAIR-AN & autoimmune). Age, BMI, waist circumference, WHR, FBS, PPBS, and fasting insulin indicate the significance of anthropometry and laboratory evaluation in diagnosing AN and MetS. Thus, it would be relevant to many developing countries with poor resources, such as those in South Asia, which are battling a rapid increase in diabetes, obesity, and other components of the metabolic syndrome. AN is a clinical marker of metabolic syndrome, and the dermatologist plays a vital role in the diagnosis and evaluation.

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