Original Article

Association Between Acanthosis Nigricans and Cardiometabolic Risk Among Overweight and Obese Patients Admitted to the Teaching Hospital Jaffna

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Abstract

Acanthosis nigricans is strongly associated with obesity and insulin resistance. This cross-sectional analytical hospital-based study is conducted to access the Association Between Acanthosis Nigricans (AN) and cardiometabolic risk among overweight and obese patients aged 18 and above admitted to medical wards of Teaching Hospital Jaffna. Data were entered and analysed using Statistical Packages for social sciences (SPSS) version 21.

Out of the 230 overweight and obese patients 74.8% had AN. Patients with AN had a higher mean BMI value of 29.65 suggesting that significant percentage of patients with AN are obese rather than being overweight. Higher prevalence of AN among females were noted. Presence of skin tags revealed an important association with AN. Most of the participants had central obesity regardless whether they were overweight or obese.

Even though statistically insignificant, individuals with AN had increased likelihood of having metabolic syndrome and associated with smokers. A significant association between Sagittal Abdominal Diameter(SAD) and presence of AN were noted. The mean of sagittal circumference in those with AN and those without respectively are 22.02 and 20.43. In conclusion AN is strongly associated with higher BMI (Obesity), higher waist circumference and higher sagittal abdominal diameter and metabolic syndrome and smoking demonstrated a strong association with AN.

Introduction

Acanthosis nigricans is a common dermatological condition characterized by velvety, hyperpigmented and hyperkeratotic plaques on skin (1). It is commonly encountered over the intertriginous areas such as back of the neck, axilla and groin. But it can occur over the other body parts like elbows, knees and mucus membranes as well but its spares the palms and soles. Presence of acanthosis nigricans over the neck as the commonest site is clinically important because of easy accessibility to diagnose (2). Two most common medical disorders associated with acanthosis nigricans are obesity and diabetes mellitus. (3,4,5) Insulin resistance is the key factor in the pathogenesis of acanthosis nigricans in these patients (6).

Obesity is considered as a chronic disease which is increasing in prevalence globally (7). Rise in obesity prevalence is associated with a significant increase in morbidity (including diabetes mellitus, hypertension, dyslipidaemia, heart disease, stroke etc) and mortality globally (6,8). Most of the metabolic complications of obesity are driven by insulin resistance which is commonly associated with acanthosis nigricans and skin tags irrespective of the cause for insulin resistance (9). Jaffna is believed to be a land of traditional values and healthy lifestyle practices in view of active lifestyle, farming and healthy dietary practices (10). This study aims to determine the association between acanthosis nigricans and cardiometabolic risk among overweight and obese patients admitted to Teaching Hospital Jaffna.

Methodology

It is a hospital-based cross-sectional analytical study as hypothesis testing was performed using cross-sectional data. The study was designed to be conducted in the medical wards of Teaching Hospital Jaffna for four months from March 2022. Overweight and obese

patients with and without acanthosis nigricans above the age of 18 years admitted to the Teaching Hospital of Jaffna were recruited for this study. The adult population above the age of 18 years is selected because studies had shown that acanthosis nigricans are commoner among the adult population. Since this study was designed to evaluate the features of obesity-related insulin resistance, the study population selected were overweight and obese patients.

Data were entered in Statistical Packages for social sciences (SPSS) version 21 was used for statistical analysis. Descriptive statistics were performed using mean (±SD) and/or median (interquartile range) for numerical variables and numbers and percentages for categorical variables. Appropriate graphs were used to present the distribution of data. The significance of the association was assessed at a 5% critical level. Unadjusted measures of risk were obtained using a chi-squared test or t-test or one-way ANOVA or non-parametric tests depending on the type of variables compared and the distribution of data. Logistic regression was performed to obtain the adjusted measures of risk. Cut off p-value to consider adding a variable to the logistic regression model is a 5% level of significance.

Results

This study recruited 230 patients in the medical wards of Teaching Hospital, Jaffna from March 2022 to June 2022. Among all the participants, 74.8% were with Acanthosis nigricans (AN+) and the remaining were without Acanthosis nigricans (AN-). Patients' age ranged from 30 to 80 years with a mean age of 56.08 ± 11.85 years. The gender ratio between males and female is 1: 1.23. The majority (95.2%) of the participants are Tamil. Around 78% of them were married and 15.7% were widowed. 78.7% of the participants completed their secondary education and 14.8% completed their primary education level. All the participants were obese and overweight with a mean BMI of 29.17 (SD = 3.7) [Table 1].

According to the statistical analysis of anthropometric data, there is a significant difference between the groups AN+ and AN- as to BMI (p=0.0001), sagittal diameter (p=0.034), and skin tags (p=0.0001), which shows that patients with AN are mostly obese [Table 1].

Table 1: Distribution of socio-demographic factors and anthropometric measurements.

Parameters	Types	Total	AN +	AN -	P value
N		230	172	58	
Mean age		56.08 ± 11.85 years	55.36 ± 12.39 years	58.22 ±1.41 years	0.112
Male: female		1: 1.23	1:1.49	1: 0.7	0.014
Ethnicity	Tamil	95.2%	93.6%	100%	0.054
	Muslim		4.1%		
	burgher		2.3%		
Marital status	Married	78%	74.1%	89.7%	0.032
	Unmarried		5.9%		
	Divorced		0.6%	5.1%	
	Widowed	15.7%	19.4%	5.2%	
Education	No schooling		2.3%		0.719
	Primary	14.8%	14.5%	15.5%	
	Secondary	78.7%	76.7%	84.5%	
	Higher		6.4%		
Income	<50000		89.5%	98.3%	0.053
	50000-100000		8.1%	1.7%	
	>200000		2.3%		
Smoking	Yes		5.4%	13.8%	0.031
	no		94.6%	86.2%	
Height in cm			158.65 ± 8.8	161.26 ± 6.9	0.055
Weight in kg			74.93 ± 13.7	72.11 ± 8.5	0.107
Waist circumference in cm			100.37 ± 9.4	98.96 ± 5.3	0.323
Sagittal diameter in cm			22.02 ± 5.2	20.43 ± 3.6	0.034
Neck circumference in cm			42.17 ± 32.07	40.97 ± 13.9	0.768
BMI			29.65 ± 3.9	27.7 ± 2.5	0.0001
Skin tags	Presence		53.0%	7.4%	0.0001
	Absence		21.7%	17.8%	

Physical activity among the participants was calculated according to the IPAQ and the physical activity profile was categorized according to the score. Figure 1 showed the trend of the profile of physical activity with and without acanthosis nigricans.
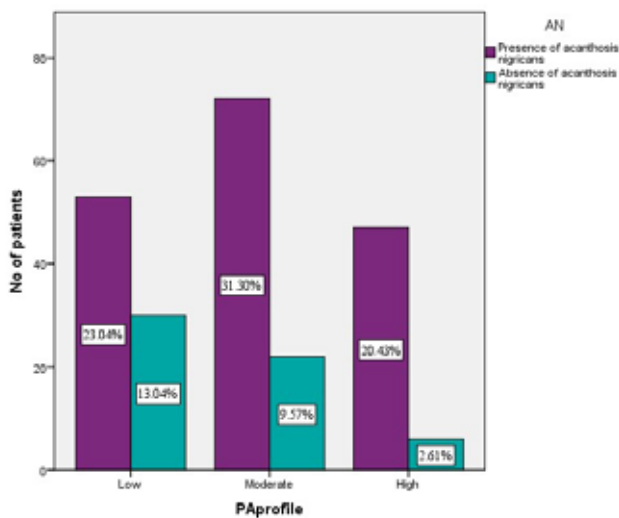
Figure 1: Illustration of physical activity profile

Table 2: Likelihood ratio of clinical features with acanthosis nigricans

Effect	Model Fitting Criteria	Likelihood Ratio Tests	
	-2 Log Likelihood of Reduced Model	Chi-Square	p-value
Age	182.470	.311	.577
Waist circumference	182.859	.700	.403
M1	182.956	.797	.372
M2	183.174	1.015	.314
M3	182.358	.199	.656
M4	183.226	1.067	.302
M5	182.253	.094	.759
Metabolic syndrome	183.139	.980	.322
Physical activity profile	200.723	18.564	.000
Skintags	211.499	29.340	.000

The likelihood ratio tests conducted to determine the association between clinical features of obesity-related insulin resistance (IR) and acanthosis nigricans (AN) yielded several notable results:

1. **Physical Activity Profile and Skintags**: These variables showed a significant association with AN, as indicated by their low p-values ($p < .001$). Participants with higher levels of physical activity and those with skintags were more likely to exhibit AN. (Table 2)

2. **Male Gender**: The variable "Male" also showed a significant association with AN ($p = .003$),

suggesting that males were more likely to have AN compared to females in the sample population. (Table 3)

3. **Other Clinical Features**: Variables such as Age, Waist Circumference, BMI of more than 35, and Neck Circumference of more than 40cm did not show a significant association with AN, as their p-values were greater than the conventional threshold of .05.

4. **Metabolic Syndrome**: Although not statistically significant ($p > .05$),"Metabolic Syndrome" showed some degree of association with AN, with p-values close to the significance threshold.

Overall, the findings suggest that certain clinical features, including high physical activity profile, skintags, and male gender, are associated with the presence of AN among individuals with obesity-related IR. However, other factors such as age, waist circumference, BMI, and neck circumference do not appear to have a significant independent association with AN in this model.

Table 3: Association between cardiometabolic risk factors and the presence of acanthosis nigricans

Cardio metabolic risk factor	AN + (N=172)	AN- (N=58)	P value
DM	47.7%	62.1%	0.069
HT	75.9%	77.6%	0.693
DL	64.5%	68.4%	0.710
Metabolic syndrome	80.2%	91.4%	0.05
Smoking	94.8%	86.2%	0.031

The chi-square test results provide insights into the association between cardiometabolic risk factors and the presence of acanthosis nigricans (AN) among the study population.

1. **Diabetes Mellitus (DM)**: While there was a trend towards a lower prevalence of DM among individuals with AN compared to those without AN (47.7% vs. 62.1%), the difference was not statistically significant ($p = 0.069$).

2. **Hypertension (HT), Dyslipidaemia (DL)** : The prevalence rates of these cardiometabolic risk factors were comparable between individuals with

and without AN, as indicated by non-significant p-values (> 0.05).

3. **Metabolic Syndrome**: A significantly higher proportion of individuals with AN had metabolic syndrome compared to those without AN (80.2% vs. 91.4%, p = 0.05), suggesting a potential association between AN and metabolic syndrome.

4. **Smoking**: The prevalence of smoking was significantly higher among individuals with AN compared to those without AN (94.8% vs. 86.2%, p = 0.031), indicating a possible association between smoking and the presence of AN.

Overall, while some cardiometabolic risk factors such as diabetes mellitus, hypertension, and dyslipidaemia did not show significant associations with AN, there were significant associations observed with metabolic syndrome and smoking. These findings suggest that individuals with AN may have an increased likelihood of having metabolic syndrome and being smokers, highlighting the potential importance of addressing these factors in the management and prevention of AN and associated cardiometabolic complications.

Table 4: Logistic regression of cardiometabolic risk factors with anthropometric measurements

Model	Unstan-dardized Coefficients		Standard-ized Coef-ficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	2.086	.363		5.741	.000
Sagittal	-.007	.006	-.075	-1.045	.297
BMI	-.034	.013	-.290	-2.678	.008
Waist circumference	.001	.004	.029	.403	.687
Neck circumference	.000	.001	-.028	-.433	.666

In the logistic regression analysis, the coefficients provide insights into the association between cardiometabolic risk factors and anthropometric measures among overweight and obese patients.

BMI: The coefficient for BMI is -0.034, with a standardized coefficient (Beta) of -0.290. This suggests that for each unit increase in BMI, the log odds of having cardiometabolic risk factors decrease by 0.034 units after controlling for other variables. The standardized

coefficient indicates that BMI has a relatively strong negative association with cardiometabolic risk factors.

Sagittal Abdominal Diameter, Waist Circumference, and Neck Circumference: These variables (Sagittal, Waist circumference, and Neck circumference) do not appear to have a statistically significant association with cardiometabolic risk factors among overweight and obese patients, as indicated by their non-significant p-values (>.05). The coefficients for these variables are close to zero, indicating minimal impact on the log odds of cardiometabolic risk factors after accounting for other variables. (Table 4)

Overall, these findings suggest that among overweight and obese patients, BMI is a significant predictor of cardiometabolic risk factors, with higher BMI values associated with lower odds of having these risk factors. However, sagittal abdominal diameter, waist circumference, and neck circumference do not seem to have a significant independent association with cardiometabolic risk factors in this model. It's important to consider additional factors and conduct further research to fully understand the relationship between anthropometric measures and cardiometabolic health in this population.

Discussion

Acanthosis nigricans and skin tags are commonly associated with insulin resistance regardless of its cause. Insulin resistance is defined as subnormal glucose response to endogenous and/ exogenous insulin. Though the causes for insulin resistance are numerous such as obesity, stress, pregnancy, lipodystrophy, insulin antibodies and medications like HAART, oral contraceptives, and steroids, insulin resistance most commonly observed in association with obesity. In this study, among 230 overweight and obese patients' majority of the patients had acanthosis nigricans. (74.8%). Patients with the presence of acanthosis nigricans have a higher mean BMI value of 29.65 suggesting that significant percentage of patients with acanthosis nigricans are obese rather than being overweight. There is a significant association between gender and acanthosis nigricans also noted in this study with the higher prevalence of acanthosis nigricans among females compared to males.

Clinical detection of acanthosis nigricans is very important because it is associated with various systemic metabolic abnormalities. Two most common medical disorders associated with acanthosis nigricans are obesity and diabetes mellitus. The consequences of obesity – related insulin resistance are diabetes mellitus, coronary artery disease and metabolic syndrome. To date there are several studies which have evaluated the prevalence of acanthosis nigricans among different population from various parts of the world. They have also evaluated the association between acanthosis nigricans and type 2 diabetes mellitus, its risk factors, atherosclerosis, and metabolic derangements. This study differs in particular from the other studies done previously is that its direct correlation with Acanthosis Nigricans and selected cardiometabolic risk factors namely Diabetes Mellitus, Hypertension, Metabolic syndrome. The selected study population is a previously unevaluated different ethnic group. Smoking and sedentary lifestyle with acanthosis nigricans also was studied. In this study we could be able to demonstrate that individuals with AN may have an increased likelihood of having metabolic syndrome and being smokers, highlighting the potential importance of addressing these factors in the management and prevention of AN and associated cardiometabolic complications. Unfortunately, we were unable to prove a statistically significant association of other cardiometabolic risk factors named Diabetes Mellitus, Hypertension, and low physical activity profile as a marker of sedentary lifestyle with presence of acanthosis nigricans.

Sagittal abdominal diameter, a novel anthropometric measure is a reliable indicator of visceral adiposity and shows a stronger correlation to cardiovascular risk and other risk factors in metabolic syndrome than other traditional anthropometric measures such BMI and waist circumference. (11) (6). We found a significant association between sagittal diameter and presence of acanthosis nigricans. The mean of sagittal circumference in those with acanthosis nigricans is 22.02 and 20.43 in those without acanthosis nigricans. But in our study, we could not be able to demonstrate a statistically significant association of sagittal abdominal diameter (SAD) with cardiometabolic risk factors as listed. It could be explained to the fact that studies have shown that when sagittal abdominal diameter is >30cm,

it is significantly associated with cardiometabolic risk factors. But our study population demonstrated an overall low SAD value, lesser than 30cm.

The results for BMI and large neck circumference are the same for other anthropometric measurements suggesting no statistically significant correlation to cardiometabolic risk factors.

Further studies required to evaluate the significance of the association between anthropometric measurements and cardiometabolic risk factors.

Conclusion

Acanthosis Nigricans is strongly associated with higher BMI (Obesity), higher waist circumference and higher sagittal abdominal diameter.

Among all the cardiometabolic risk factors tested, metabolic syndrome and smoking demonstrate a strong association with acanthosis nigricans. However statistically significant correlations between acanthosis nigricans were not made with other cardiometabolic risk factors such as diabetes mellitus, dyslipidemia, hypertension, and sedentary lifestyle. These results could be explained because this study was conducted in a subset of overweight and obese patients as opposed to a general population.

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