



Original Research Article

Prevalence of acanthosis Nigerians in patients with HIV infection and its relation with Metabolic Syndrome

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ABSTRACT

Introduction: According to International Diabetes Federation (IDF) prevalence of diabetes in India is 8.8%. Acanthosis Nigerians is one of the marker of insulin resistance which is easy to detect. There are not many studies which have correlated this ubiquitous clinical marker with metabolic syndrome and moreover there is no study on HIV positive patients

Aims: To study the prevalence of acanthosis Nigerians in patients with HIV-infection, attending ART clinic or admitted at a tertiary care centre and to study its relationship with metabolic syndrome.

Materials and Methods: This is a cross sectional observational study done for 18 months including 300 patients. All patients with HIV-infection attending ART clinic or admitted were included in the study.

Results: Acanthosis Nigerians was found more in males as compared to females (15.35 vs 9.52%) though the difference was not statistically significant while metabolic syndrome was found in 12.7% of the patients. Comparative analysis of anthropometric data of metabolic syndrome patients with and without acanthosis Nigerians revealed larger waist circumference in patients with acanthosis Nigerians (85.44 vs 81.75) and it was statistically significant (p value 0.037). Sensitivity and specificity analysis of acanthosis Nigerians and metabolic syndrome revealed low sensitivity of acanthosis Nigerians in predicting presence of metabolic syndrome (17 %) and low positive predictive value (18.42 %). However it revealed high specificity (87.98 %) and a negative predictive value (86.97 %). Odds ratio of metabolic syndrome in presence of acanthosis Nigerians was 1.5. The CD4 count values were not significantly different in those with or without acanthosis Nigerians. The age, sex, duration of the therapy or the ART regimen did not statistically influenced occurrence of acanthosis Nigerians

Conclusion: Acanthosis Nigerians is a common and easily accessible dermatological condition. Increased waist circumference and waist hip ratio are strong predictors of acanthosis Nigerians. Acanthosis Nigerians can be used to predict occurrence of metabolic syndrome with high specificity and patients should be thoroughly evaluated for metabolic syndrome in its presence.

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1. Introduction

The burgeoning epidemic of obesity and diabetes will be defining features of healthcare challenges in the 21st century. Worldwide, the proportion of adults with a body-mass index (BMI) of 25 kg/m² or greater increased between 1980 - 2013 from 28.8% (95% UI 28.4–29.3) to

36.9% (36.3–37.4) in men, and from 29.8% (29.3–30.2) to 38.0% (37.5–38.5) in women. Prevalence has increased substantially in children and adolescents in developed countries; 23.8% (22.9–24.7) of boys and 22.6% (21.7–23.6) of girls were overweight or obese in 2013. The prevalence of overweight and obesity has also increased in children and adolescents in developing countries, from 8.1% (7.7–8.6) to 12.9% (12.3–13.5) in 2013 for boys and from

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8.4% (8.1–8.8) to 13.4% (13.0–13.9) in girls.¹ According to the National Family Health Survey (NFHS) in India, the percentage of ever-married women aged 15–49 years who are overweight or obese increased from 11% in NFHS- 2 to 15% in NFHS-3.² In India, many studies have shown that the prevalence of overweight among adolescents varies between 10% and 30%.³ There is marked geographical variation in prevalence of diabetes. The prevalence is lowest in rural areas of developing countries, it is generally intermediate in developed countries, and is highest in certain ethnic groups, particularly those that have adopted Western lifestyle patterns. The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014. The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014.⁴ Prevalence of diabetes in India is 8.8% according to International Diabetes Federation (IDF).

It is estimated that the onset of diabetes occurs an average of about 4–7 years before clinical diagnosis based on symptoms, and that one-third to one-half of individuals with type 2 diabetes are undiagnosed at any given time.⁵ In the general population, several metabolic risk factors are strongly interrelated and are part of the metabolic syndrome (MS) as was described⁶ in 1988. Metabolic syndrome is a constellation of derangements in glucose, insulin, and lipid metabolism, along with abdominal obesity. The National Cholesterol Education Program (NCEP) has endorsed the importance of the metabolic syndrome in cardiovascular risk assessment by introducing a case definition of MS based on clinically easily obtainable anthropometric and laboratory parameters.⁷ Metabolic syndrome affects 24 percent of the adult population in the U.S.⁸ and 15 percent of non-diabetic adult Europeans and is associated with an increased risk of CVD.⁹ Metabolic syndrome is associated with abdominal obesity, but absolute or partial lack of body fat may result in a similar metabolic risk profile. It is therefore important to recognise markers of insulin resistance and be proactive in advising lifestyle changes to obese individuals with these markers and also keep them under follow up for introduction of drug therapy for diabetes as soon as it clinically manifests.

Acanthosis Nigricans is one such marker of insulin resistance which is easy to detect. However there are not many studies which have correlated this ubiquitous clinical marker with metabolic syndrome. And moreover there is no study on HIV positive people. It is particularly relevant in this population where both the disease and its treatment predispose to dyslipidemia and where in future the highest cause for mortality will be cardiovascular disease.

2. Materials and Methods

This was a cross-sectional observational study conducted in the department of General Medicine, Government Medical College Nizamabad, T.S. Total duration of study was 18

months from July 2019 to December 2020. It was divided into initial 1 year for collection of data and later 6 months for analysis of results. All patients with HIV-infection attending ART clinic or admitted were included in the study.

Prevalence of metabolic syndrome (MS) in HIV varies from 14–20%. Acanthosis Nigricans (AN) is seen in 30–60% cases of metabolic syndrome. For calculation of sample size a prevalence of 15% & 40% was taken for metabolic syndrome and acanthosis Nigricans respectively. Expected prevalence of acanthosis Nigricans in metabolic syndrome was 6% (40% of 15%). It was found that for the expected result of 6% (range 3–9%) with 95% confidence level, a sample size of 271 will be required. Therefore, a sample size of 300 was chosen for this study.

2.1. Inclusion criteria

All adult patients (> 18yrs) with HIV infection attending ART clinic or admitted were eligible for inclusion in the study.

2.2. Exclusion criteria

Patients who met any of following criteria were excluded; – Patients on corticosteroid therapy, patients diagnosed with diseases of adrenal gland, patients with known thyroid dysfunction including tumour or surgery

Metabolic syndrome (NCEP ATP III criteria) is defined by presence of three or more of the following criterias

1. Abdominal obesity, given as waist circumference Men>102cm /women>88cm.
2. Triglycerides >150mg/dl.
3. HDL cholesterol; Men <40mg/dl/Women < 50 mg/dl.
4. Blood pressure >130/>85 mmhg.
5. Fasting glucose 110 mg/dl.

Acanthosis Nigricans was defined as benign and common condition characterised by velvety, hyperpigmented plaques in the skin

Patients with HIV attending ART OPD or admitted in ward were screened for presence of acanthosis Nigricans. Written informed consent was taken from all the patients. Anthropometric measurements of selected patients: height, weight, BMI, waist circumference, hip circumference were measured and recorded. Waist circumference was measured at midway between iliac crest below and subcostal margins above, with the help of flexible measuring tape. Hip Circumference was taken at the level of greater trochanter. Patients were examined at neck, axilla, knuckles, cubital and popliteal fossae and other intertriginous areas for presence of acanthosis Nigricans. The lab parameters; fasting and post prandial blood glucose, HbA1c in selected case, Total cholesterol, HDL, LDL, Triglycerides, CBC, RFT, LFT, CUE, were noted from patient records if they were done within last three months otherwise fasting samples were

drawn next day. The subjects were screened for presence of metabolic syndrome based on NCEP ATP-III criteria.

2.3. Statistical data analysis

The data on categorical variables is shown as n (% of cases) and the data on continuous variables is presented as Mean and Standard deviation (SD). The intergroup comparison of categorical variables was done using Chi-square test. Sensitivity, specificity, positive predictive and negative predictive value was calculated with the help of 2 x 2 contingency table. The p-values less than 0.05 are considered to be statistically significant. All the hypotheses were formulated using two tailed alternatives against each null hypothesis (hypothesis of no difference). The entire data was statistically analyzed using Statistical Package for Social Sciences (SPSS ver 21.0, IBM Corporation, USA) for MS Windows.

3. Results

Two ninety nine patients were available for analysis. 72% were males and 28 % were females. Most of the patients were in 4th (27%) and 5th (32%) decade of life.

Acanthosis Nigerians was found in 41 patients i.e., 13.7% of total patients. It was found more frequently in males as compared to females (15.35 vs 9.52%) though the difference was not statistically significant.

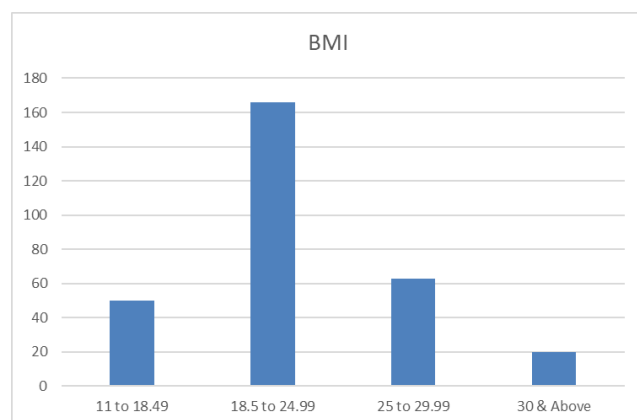


Fig. 1: Distribution of patients on basis of BMI.

Analysis of BMI revealed that most of the patients (72.2%) were of BMI < 25Kg/m², 21% of the patients were overweight (BMI 25-29.9Kg/m²) and only 6.7 % patients met the criteria for obesity (BMI ≥ 30kg/m²).

Waist Circumference in females was found to be more than 88cms in only 5 females and it was less than 88cms in 79 females. In males waist circumference more than 102cm was found in 7 patients and was less than 102cm in 208 patients.

The CD 4 count was less than 500cells/cmm in 66.5 % of patients.

The patients with metabolic syndrome (n=38) were divided into two groups on basis of presence (7/38) or absence (31/38) of acanthosis Nigerians, comparison of these two groups revealed that patients of metabolic syndrome with acanthosis Nigerians have higher age 49.29 ± 10.77 (Mean $\pm$ SD) vs 41.52 ± 9.80 (Mean $\pm$ SD) and BMI (27.35 vs 25.36) when compared to patients of metabolic syndrome without acanthosis Nigerians, these difference were not statistically significant. However, in these two groups statistically significant difference in waist circumference (97.4 vs 86.5cm) and WHR (1.05 vs 0.94) (p value < 0.03 and 0.005 respectively) was observed.

Patients without metabolic syndrome (n=261) were also divided into two groups on the basis of presence or absence of acanthosis Nigerians. Comparative analysis of anthropometric data of these 2 groups revealed a larger waist circumference in patients with acanthosis Nigerians (85.44 vs 81.75cm) and it was statistically significant (p value 0.037).

Larger waist circumference was found in patients of acanthosis Nigerians irrespective of presence or absence of metabolic syndrome and this indicates that abdominal obesity is an independent risk factor for acanthosis Nigerians. Both waist circumference and waist hip ratio are significantly associated with acanthosis Nigerians in patients with metabolic syndrome however no of patients in this subset was low (n=38).

Sensitivity and specificity analysis of acanthosis Nigerians and metabolic Syndrome revealed low sensitivity of acanthosis Nigerians in predicting presence of metabolic syndrome (17%) and low positive predictive value (18.42%). However it revealed high specificity (87.98%) and a negative predictive value (86.97%).

All the patients were divided in two groups as those with acanthosis Nigerians and those without it. They were analysed with t test to find any association with presence of acanthosis Nigerians. The mean BMI was found to higher in patients with acanthosis Nigerians and was found to be statistically significant. However the mean age, CD4 counts, duration of disease & therapy, ART regimen were not found to be significantly different between the 2 groups.

2x 2 contingency table for presence or absence of acanthosis Nigerians with respect to BMI more than and less than 30 kg/m². As depicted in table above. In cases with BMI more than 30 kg/m² odds ration for acanthosis Nigerians was found to be 1.6.

4. Discussion

Acanthosis Nigerians (AN) is frequently seen in cases at risk of metabolic syndrome. However, prevalence of acanthosis Nigerians and its utility for diagnosing metabolic syndrome is not well known in patients with HIV infection. This study was conducted with primary objective of finding the prevalence of acanthosis Nigerians in patients of HIV,

Table 1: Prevalence of acanthosis Nigerians in males and females.

Acanthosis Nigerians	Sex		Total
	Female (n=84)	Male (n=215)	
Present	8	33	41
Total	84	215	299
Prevalence Rate	0.0952	0.1535	0.1371
Prevalence Rate as Percent	9.52	15.35	13.71
95% C.I.	(0.08, 0.11)	(0.14, 0.17)	(0.12, 0.15)
95% C.I. as Percent	(7.68, 11.37)	(13.61, 17.09)	(12.37, 15.05)

Table 2: Comparison of anthropometric data of patients of metabolic syndrome with and without acanthosis Nigerians.

Variable	Acanthosis (subjects with metabolic syndrome n = 38)			
	Present Mean(SD)	Absent Mean(SD)	P value	Significant if P <0.05
Age (yrs)	49.29 (10.77)	41.52 (9.80)	0.071	No
BMI (Kg/M ²)	27.35 (4.56)	25.36 (4.37)	0.287	No
Waist (cm)	97.43 (10.64)	86.55 (11.64)	0.03	Yes
WHR	1.05 (0.11)	0.94 (0.08)	0.005	Yes
Males	4 (10.5%)	23 (60.5%)		N.A.

Table 3: Comparison of anthropometric data of patients without metabolic syndrome with and without Acanthosis Nigerians.

Acanthosis Nigerians in subjects without metabolic syndrome n =261)				
Variable	Present	Absent	P value	Significance
Age	41.62 (9.81)	41.12 (12.10)	0.82	No
BMI	23.60 (4.35)	22.41 (4.31)	0.136	No
Waist	85.44 (8.90)	81.75 (9.66)	0.037 < 0.05	Yes
WHR	0.92 (0.08)	0.92 (0.07)	0.73	No
Males	29 (11.1%)	159 (60.9%)	0.065	No

Table 4: Two by two analysis of Acanthosis Nigerians and Metabolic Syndrome

Acanthosis Nigerians and Metabolic Syndrome Cross tabulation				
		Metabolic Syndrome		Total
		No	Yes	
Acanthosis Nigerians	No	227 (d)	31 (b)	258
	Yes	34 (c)	7 (a)	41
Total		261	38	299

and its relation with metabolic syndrome. Two ninety-nine patients were available for analysis as one patient was lost to follow up. Most of the patients were in 4th and 5th decade of life (27% and 32% respectively). Males were more frequent in study population than females (72 vs 28 %) in our study.

Prevalence rate of acanthosis Nigerians in males and females was 15.35 % and 9.52% respectively though the difference was not statistically significant. 2% of the patients were overweight and 6.7% were obese. In present study metabolic syndrome (MS) was found in 12.7% (n=38) of the patients. Metabolic syndrome is a common complication in patients of HIV with prevalence rate varying from 12-40 %.¹⁻⁴ Previous studies have reported a highly varied prevalence of acanthosis Nigerians in different ethnic groups, black people being more commonly affected compared to white people. Stuart et al for the first time reported the prevalence of acanthosis Nigerians in an unselected population, varied from 7% and 30%–40% in

adolescents and adults respectively.¹⁰ Burke et al reported this figure to be 41.1% in diabetic patients and 31.6% in healthy subjects Dassanayake and colleagues found a prevalence of 17% in urban population in Sri Lanka. Grandhe et al found a significantly higher prevalence of acanthosis Nigerians among Indian diabetic patients (62.6%) when compared with healthy subjects (40%). The highest prevalence of acanthosis Nigerians (74%) was reported by Hud et al in a subset of obese population.¹¹ The prevalence of acanthosis Nigerians found in our study was within the range described in different populations in past studies. However, it is perhaps first study on acanthosis Nigerians in HIV patients to the best of our knowledge. Many studies have been conducted on metabolic syndrome in patients of HIV infection. The prevalence rates of metabolic syndrome in HIV patients in published studies vary from 10.1% to 45.4%.¹¹⁻¹⁹ Various Indian studies have reported prevalence of metabolic syndrome in general

Table 5: Analysis of association of various factors with Acanthosis Nigerians

		Levene's Test for Equality of Variances		t-test for Equality of Means		
		F	Sig.	t	df	P value (2-tailed)
CD4	Equal variances assumed	0.813	0.368	-0.282	296	0.778
	Equal variances not assumed			-0.26	50.706	0.796
BMI	Equal variances assumed	0	0.993	-1.976	297	0.049
	Equal variances not assumed			-1.931	52.635	0.059
Age	Equal variances assumed	0.857	0.355	-0.898	297	0.37
	Equal variances not assumed			-0.996	58.288	0.323
AZT (zidovudine)	Equal variances assumed	2.628	0.11	0.24	67	0.811
	Equal variances not assumed			0.302	18.425	0.766
TDF (Tenofovir)	Equal variances assumed	0.624	0.431	0.543	227	0.588
	Equal variances not assumed			0.64	48.491	0.525
PI	Equal variances assumed	0.686	0.411	-0.476	53	0.636
	Equal variances not assumed			-0.415	10.197	0.687
EFV (Efavirenz)	Equal variances assumed	1.276	0.26	0.773	185	0.44
	Equal variances not assumed			0.926	44.649	0.359
NVP (Nevirapine)	Equal variances assumed	0.204	0.652	0.19	297	0.85
	Equal variances not assumed			0.213	59.028	0.832
Duration of Therapy	Equal variances assumed	0.934	0.335	0.091	297	0.928
	Equal variances not assumed			0.108	62.49	0.915
Duration of disease	Equal variances assumed	.006	.939	-.694	297	0.488
	Equal variances not assumed			-.753	57.146	.455

Table 6: Cross tabulation of BMI and Acanthosis Nigerians

BMI kg/m ²	Acanthosis igerians		Total
	No	Yes	
BMI < 30	242d	37c	279
BMI > 30	16b	4a	20
Total	258	41	299

population between 3% and 25%.^{20,21} The prevalence of metabolic syndrome found in our study was 12.7 % which is within the described range.

Anuradha S Dassanayake et al in Sri Lanka investigated the prevalence of acanthosis Nigerians among adults in an urban Sri Lankan community and described its utility to detect metabolic syndrome.²² The sensitivity, specificity, positive predictive value and negative predictive value of acanthosis Nigerians to detect metabolic syndrome were 28.2%, 89.0%, 45.9% and 79.0% for males, and 29.2%, 88.4%, 65.6% and 62.3% for females, respectively. One study was done at Chennai in India to find out sensitivity and specificity of acanthosis Nigerians as a skin marker of metabolic syndrome,²³ it reported sensitivity 62.50% (48.36, 74.78), Specificity 94.23% (84.36, 98.02), positive predictive value 90.91%, negative predictive value 73.13%, of acanthosis Nigerians in detecting metabolic syndrome. However the sample size was only 100 in this study. Considering exclusion criteria of history of diabetes, hypertension, dyslipidemia and alcohol consumption prevalence of metabolic syndrome reported was very high (48%).

In our study we found sensitivity, specificity, positive predictive value and negative predictive value of acanthosis Nigerians to detect metabolic syndrome, 17.07%, 87.98 %, 18.42% and 86.97%. The sensitivity to detect metabolic syndrome was found to be lower in our study. However, the negative predictive value found in our study was significantly higher. This results were similar to ones reported by Dassanayake et al.²² In comparison with study done by Balaji et al²³ we found lower prevalence of acanthosis Nigerians and metabolic syndrome and similar specificity and negative predictive value. However sensitivity was lesser 17.07% vs 62.5%. The different prevalence in acanthosis Nigerians and metabolic syndrome may be due to major inherent difference in two study populations. Metabolic syndrome in patients with HIV has been described in only 3-20% of cases in India but in study conducted at Chennai prevalence of metabolic syndrome was reported as high as 46%.²³ The difference between these studies in sensitivity may be attributable to much larger sample size of our study population (300 vs 100) and lower prevalence of acanthosis Nigerians and metabolic syndrome 13.7 vs 33% and 12.7 vs 48%.

There are very limited studies over prevalence of acanthosis Nigerians in general population in India. Moreover, we could find only one study in India which evaluated significance of acanthosis Nigerians as a marker of metabolic syndrome. The sample in this study was 100. In our study we used a much larger sample size. Acanthosis Nigerians and metabolic syndrome were found fairly common in our study population, 13.7 and 12.7% of cases respectively. Acanthosis Nigerians was found to predict metabolic syndrome with a very high specificity.

5. Recommendation

In this study it was found that acanthosis Nigerians and metabolic syndrome was fairly common in patient with HIV infection. Waist hip ratio and Waist circumference were found to have strong predictive value in acanthosis Nigerians. Waist circumference was shown to be a predictor of acanthosis Nigerians even in absence of metabolic syndrome. Acanthosis Nigerians when used as a clinical tool to predict occurrence of metabolic syndrome showed a high specificity and negative predictive value but with low sensitivity. Patients with acanthosis Nigerians are at risk for all components of the metabolic syndrome such as obesity, hypertension, elevated triglycerides, low HDL, and impaired glucose tolerance. The easy detectability increases its potential to play a bigger role in detecting people at risk of metabolic syndrome. This would be relevant to many developing countries with poor resources, such as those in South Asia, which are battling with rapid increases in diabetes, obesity and other components of the metabolic syndrome.

Our study had few limitations, firstly, acanthosis Nigerians was not quantified using a standard scale and only its presence or absence in the neck was noted, this might be a subject for future studies, secondly, NCEP ATP 3 criteria was used for diagnosis of metabolic syndrome. Since it was done on Indian patients, South Asian modification of NCEP ATP 3 could have been more appropriate diagnostic criteria.

6. Conclusion

Acanthosis Nigerians is a common and easily accessible dermatological condition. Increased waist circumference and Waist hip ratio are strong predictors of acanthosis Nigerians. Acanthosis Nigerians can be used to predict occurrence of metabolic syndrome with high specificity and patients should be thoroughly evaluated for metabolic syndrome in its presence.

7. Conflict of Interest

There are no conflicts of interest in this article.

8. Source of Funding

None.

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