



ISSN: 0976-3031

Available Online at <http://www.recentscientific.com>

International Journal of Recent Scientific Research
Vol. 6, Issue, 7, pp.4923-4926, July, 2015

**International Journal
of Recent Scientific
Research**

RESEARCH ARTICLE

ACANTHOSIS NIGRICANS IN TYPE 2 DIABETES MELLITUS PATIENTS AND ITS RELATION WITH OBESE WOMEN WITH PCOS AND BODY MASS AT A TERTIARY LEVEL HOSPITAL IN CENTRAL INDIA

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ARTICLE INFO

Article History:

Received 5th, June, 2015
Received in revised form 12th,
June, 2015
Accepted 6th, July, 2015
Published online 28th,
July, 2015

ABSTRACT

Acanthosis Nigricans (AN) as a possible marker of an increased risk for diabetes. To determine the prevalence of AN in type 2 diabetes mellitus (T2DM) and its correlation with obese women with Polycystic ovary syndrome (PCOS) and Body mass index (BMI) in Central Indians. Present work is a cross sectional open label study carried out over a period of 11 months in tertiary level hospital in Central India. A total 300 patients with T2DM were included in the study. Who were age between 18-50 years. Regression analysis was done to determine the association of AN with T2DM. AN was observed in 150 of the T2DM patients. BMI was significantly higher in the T2DM patients with AN as compared to those without AN. Among the obese PCOS patients 81% had BMI value of more than 30 kg/m² as compared to 13% of the patient who did not have AN. AN is correlated with obesity. Central Indians have high prevalence of AN and it is an independent cutaneous marker of both T2DM and BMI.

Key words:

Acanthosis Nigricans, Type 2 diabetes mellitus, Polycystic ovary syndrome, Central Indians.

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INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both¹. The 1980 WHO Expert Committee proposed two major classes of DM and named them, insulin dependent diabetes mellitus (IDDM) or type 1 DM, and non-insulin dependent diabetes mellitus (NIDDM) or type 2 DM. In the past type 2 diabetes mellitus usually developed in adults and used to be called adult-onset diabetes². However during the past twenty years there has been a marked increase in the number persons, including children, living in the United States who are overweight. Following the rise in obesity there has been a dramatic increase in type 2 diabetes in both adults and now children.

Acanthosis nigricans is most commonly associated with the disorders which are associated with insulin resistance, which include obesity, T2DM, and Polycystic Ovary Syndrome (PCOS)³. Burke *et al*⁴ proposed a classification system to grade the severity of AN and found that the severity of AN was associated with elevated fasting insulin and increased BMI. More recently, attention has turned to acanthosis nigricans

(AN) as a possible marker of increased risk for the development of diabetes. AN, a dermatologic condition characterized by hyperpigmentation, hyperkeratosis, and papillomatosis, has been shown in many cases to be associated with hyperinsulinemia. Typical areas of involvement include the posterior neck, the axilla, the elbows, and the knees; when AN is present the neck is involved 93% to 99% of the time⁵. Thus Grandhe *et al*⁶. Report that up to two-thirds of type 2 diabetic patients from North India will display this sign. While obesity increases the risk for development of AN, the differences in prevalence of AN between racial groups cannot be explained solely by differing rates of obesity⁷.

Polycystic ovary syndrome (PCOS) is one of the most common female endocrine disorders of uncertain etiology. The disorder causes multiple abnormal cysts in enlarged ovaries so they do not produce the normal no. of eggs & do not ovulate normally⁸. Apridonidze *et al*⁹, (2005) who found the only phenol typical difference between the PCOS patients with and without the MBS was the presence of acanthosis nigricans. More recently, attention has turned to obese PCOS patients with AN do not have significantly higher insulin resistance than obese patients without AN¹⁰.

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To the best of our knowledge there are no studies showing the prevalence of AN in type 2 diabetes mellitus (T2DM) and its true correlation with PCOS and body mass index in central Indians.

MATERIAL AND METHODS

This is a cross-sectional study in the patients with T2DM and PCOS. Who attended the Department of Medicine, in collaboration with Department of Gynecology & obstetrics L.N. Medical College & Research Centre, Bhopal, between July 2014 to May 2015, was carried out, after taking approval from the institutional ethics committee.

A total of 300 female patients with T2DM were included in the study. The diagnosis of diabetes mellitus was based on the Fasting Blood Sugar (FBS) and the Post Prandial Blood Sugar (PPBS) reports. Those with an FBS value of ≥ 126 mg/dL and a PPBS value of ≥ 200 mg/dL were identified as diabetics. The diagnosis of AN was done clinically by a certified physician. Included in this study were individuals 18-50 years of age with T2DM (according to the World Health Organisation (WHO) definition.

Patients complaining of irregular menses and /or infertility were enrolled as per inclusion and exclusion criteria after taking written informed consent. Presence of at least two criteria from clinical, hormonal, and abdominal USG category were considered diagnostic of PCOS. Women with complain of irregular menses or oligomenorrhea (absence of menses for 35-182 days) or amenorrhea (absence of menses for > 182 days), signs or symptoms of HA, abdominal USG showing at least 12 follicles (2-9 mm in diameter) arranged peripherally around a dense core of ovarian stroma or scattered throughout an increased amount of stroma were enrolled in the study.

Subjects were examined for the presence of AN at the neck, and its severity and texture were graded using standard scales as described by Burke *et al*⁴. Severity was graded from 0 to 4 as follows: grade 0 - not visible on close inspection; grade 1 - clearly present on close visual inspection; grade 2 - limited to base of the skull but does not extend to the lateral margins of the neck; grade 3 - extending to the lateral margins of the neck but not visible from the front; and grade 4: extending to the anterior neck. The texture of AN at the neck was graded from 0 to 3 as follows: Grade 0 - smooth to touch, no differentiation from normal skin to palpation; Grade 1 - rough to touch, clearly differentiated from normal skin; Grade 2 - coarseness can be observed visually, portions of the skin clearly raised above other areas; and Grade 3 - extremely coarse, "hills and valleys" observable on visual examination. The presence of AN at other typical sites, including knuckles, elbows, axilla and knees, was also documented. Those patients with localized hyperpigmentation without skin thickening were not considered to have AN⁴. AN was assessed by a single trained observer.

An administered questionnaire was used to collect data on: age; sex; self-reported ethnicity; Family history of T2DM; duration of T2DM; and treatment with oral hypoglycaemics, insulin or both. Body mass index (BMI) was calculated (kg/m^2), and

BMI percentile for age-and sex (BMI percentile) was determined using published gender-specific Centers for Disease Control charts¹¹. BMI percentile was classified using the Endocrine Society's 2008 guidelines: below the 85th percentile (normal), at or above the 85th percentile and below the 95th percentile (overweight), and at or above the 95th percentile (obese)¹².

RESULTS

A total of 300 patients with T2DM and PCOS, who attended the Medicine Department in collaboration with Department of Gynecology & obstetrics during between July 2014 to May 2015, were selected for the study. 150 of the T2DM patients had AN and 150 patients did not have AN.

Table No1 Acanthosis Nigricans (AN): Prevalence, and age, demographic and clinical characteristics of study sample

Characteristic	An with T2DM (n=150)	An without T2DM (n=150)	P value
Age (Years)	33.9 \pm 5.8	45.4 \pm 7.9	ns
BMI	27.5 \pm 2.2	27.2 \pm 2.3	.0224 (ns)
PCOS (%)	85%		
Family history of DM (%)	89%	52%	
Duration of T2DM (yrs) (%)	67%	32%	
Diabetes treatments (cases)	Oral 86 Oral & Insulin 45 Insulin 19	60 38 52	

Values expressed as mean \pm SD. Categorical data were expressed as percentage. using independent sample 't' test. * $P \leq 0.05$ considered significant; † $P \leq 0.001$ highly significant; AN=Acanthosis nigricans; ns=not significant.

Table No: 1 shows that there was no significant difference in the mean age among the T2DM patients. Comparison of anthropometric parameters between both groups BMI was found to be statistically not significant ($P > 0.005$) using independent sample 't' test. PCOS was observed in 85% of the T2DM patients with AN, while none of the T2DM patients without AN were found to be PCOS. A family history of DM was present in 89% of the patients with AN and in 52% of the patients without AN. Duration of T2DM was present in 67% of the patient with AN and in 32% of the patients without AN. T2DM treatment regimen.

Table No2 Acanthosis nigricans in obese vs non-obese polycystic ovary syndrome women

	Obese	Non-obese	Total
AN present	120 (80%)	14 (0.9%)	134
AN absent	30 (20%)	136 (90.1%)	166
Total	150	150	300

Table No :2 shows that 80% of obese patients had AN and in rest of patients AN is absent. 90% of AN was absent in non-obese patient and 0.9% of AN was present in non-obese patients.

Table No3 Distribution of Acanthosis Nigricans in different classes of BMI among T2DM patients.

BMI (kg/m^2)	AN (n=150)	NAN (n=150)
22.9 and less	18 (12%)	25 (16%)
23-24.9	38 (25.3%)	48 (32%)
25 and above	32 (21.3%)	56 (37.3%)
30 and above	62 (41.3%)	21 (14%)

Table No ; 3 shows that 16% of the patients without AN had a normal BMI as compared to 12 % of the patients in AN. A BMI of more than or equal to 23 kg/m² was observed in 32% of the patients NAN as compared 25% of the patients with AN. 37.3% of patients had a BMI of more than 25 kg/m² compared to 21% of the patient with AN. This study showed that 41% of the patients had a BMI of more than 30kg/m² as compared to 14% of the patients who did not have AN. This was statistically significant.

Table No 4 Distribution of Acanthosis Nigricans in different classes of BMI among PCOS patients.

BMI (kg/m ²)	AN(n=150)	NAN (n=150)
22.9 and less	03 (0.2%)	12(0.8%)
23-24.9	10 (0.6%)	71 (47%)
25 and above	15(10%)	47 (31%)
30 and above	122 (81%)	20 (13%)

Table No 4: shows that 0.8 % of patients without AN had a normal BMI as compared to .2 % of the patients in AN. A BMI of more than or equal to 23 kg/m² was observed in 47% of the patients of NAN as compared to .6% of the patient with AN. BMI was more then 25 kg/m² observed in 31% of patient in NAN as compared to 25% of the patient with AN. This study showed that 81% of the AN patient had a BMI of more than 30kg/m² as compared to 13% of the patients with NAN.

DISSCUSION

The burden of disease in Central Indians is changing. Changes in life style and work patterns and more obesity have coincided with a surge in consumption of sugary drinks, alcohol, and tobacco. As most of the T2DM subjects are obese, BMI is an important confounding factor in the association of AN with T2DM. To our knowledge, this is the first report to evaluate the sensitivity of acanthosis nigricans screening for detecting insulin resistance in Central India. Greater understanding of how acanthosis nigricans performs as a screening test can lead to its more-effective implementation in health risk assessments. Our data demonstrate that acanthosis nigricans, when it is present, has high specificity for identifying an individual with Diabetes.

In this study, it was found that among the obese with PCOS patients, 81% among the AN patients and 13% among the non Acanthosis patients had a BMI of more than 30kg/m². This implies that among the obese patients, the group with a BMI of more than 30kg/m² were more prone to develop AN. Acanthosis nigricans, a dermatologic condition which is characterized by hyperpigmentation, hyperkeratosis and papillomatosis, has been shown to be a reliable marker of hyperinsulinaemia and DM³. In a similar study which was done in South Indian reported that obese patient 58% among the AN patients and 19% among the non AN had a BMI of more than 30 kg/m²¹³. In another study reported that prevalence in the PCOS patients in India is unknown, but in a study in Iraq, a high prevalence of AN of upto 68% was observed in the PCOS patients¹⁴.

The current study shows that T2DM patient 41% among the AN patients and 14% among the non AN patients had a BMI of more than 30kg/m². The above findings were similar to

pervious studies. N P Grandhe⁶ found significantly higher prevalence of AN among diabetic patients (62.6%) when compared with healthy subjects (40%). Apart from the higher prevalence, diabetic patients had more severe grades of AN when compared with healthy subjects. The higher prevalence of AN both in diabetic as well as healthy subjects in our study can be explained by the ethnic predisposition. A Trinidad-based study, reported that a relatively high manifestation of AN among diabetic patients was found - as many as 1 in 2 diabetic patients had AN. Of note, AN was 20% more likely to manifest in diabetic patients of East Indian than African or mixed origin – possibly due to a higher prevalence of ectopic fat and associated insulin resistance in the former¹⁵. In another study, a high BMI was significantly associated with the prevalence of T2DM and a significant number of patients with T2DM had AN¹⁶.

In this study We found the prevalence of AN to be high across age groups although we did observe a steady decrease in the prevalence of AN with increasing age. Formal recommendations of the American Diabetes Association (ADA) have recognized AN as a risk factor for T2DM in children and adolescents and have incorporated it into formal risk Assessment protocols since 2000. Stuart *et al*¹³ reported lower prevalence of AN in people over 50 years, whereas no such age related difference was found in our study.

In our study, 85% of the T2DM also had obese with PCOS patients along with AN, which indicated that obesity was a common risk factor for both DM and AN. A close association between obesity and AN were found in other studies¹⁷. 89% patients with AN had a history of T2DM in the first degree relatives and 52% among the patients without AN had a history of DM running in their first degree relatives. The results of our study was similar to earlier studies¹³. N P Grandhe⁶ reported no evidence (p > 0.40) of an age-, BMI adjusted association between AN and a history of a family history of T2DM, T2DM treatment regimen, the duration of T2DM or the RBG. Similarly to our study results.

CONCLUSION

Central Indians have higher prevalence of AN, and it is a cutaneous marker of both T2DM and BMI independent of each other. This study presents consistent evidence of high rates of AN and of association of AN with the risk of diabetes and with insulin resistance. Because AN is a identifiable marker of risk for diabetes among PCOS. There is a need to increase awareness regarding obesity as well as AN, as very few patients were aware of their abnormal BMI and none was aware of skin discoloration. This might help in stimulation discussion on

Lifestyle modifications.

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How to cite this article:

VibhuNarainKhanna., Acanthosis Nigricans In Type 2 Diabetes Mellitus Patients And Its Relation With Obese Women With Pcos And Body Mass At A Tertiary Level Hospital In Central India. *International Journal of Recent Scientific Research* Vol. 6, Issue, 7, pp.4923-4926, July, 2015
