Endocrinology Section

Acanthosis Nigricansin PCOS Patients and Its Relation with Type 2 Diabetes Mellitus and Body Mass at a Tertiary Care Hospital in Southern India

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ABSTRACT

Background: Acanthosis nigricansis was viewed recently as a possible marker of an increased risk for diabetes. Acanthosis Nigricans (AN) can help in identifying the patients with an increased risk for Type 2 Diabetes Mellitus (T2DM) among Polycystic Ovary Syndrome (PCOS) cases. Hence, this study was carried to know the prevalence of AN in PCOS and its correlation with diabetes mellitus and the body mass.

Methods: A prospective, longitudinal study in the patients with PCOS, who attended the Department of Medicine, Kasturba Medical College [KMC] Hospital, Attavar, Mangalore, Karnatka, India between December 2008 to April 2010, was carried out. A total of 119 patients with PCOS were included in the study. A complete history, along with the demographic data of the patients who were aged between 15-35 years, were considered for the analysis.

Results: AN was observed in 56% of the PCOS patients. The Body Mass Index (BMI) and the waist circumference were significantly higher in the PCOS patients with AN, as compared to those without AN. Among the 119 PCOS patients,77% were found to have BMI values which were above the normal. Among the obese PCOS patients, 58% had BMI values of more than 30kg/m^2 as compared to 19% of the patients who did not have AN. Type 2 DM was observed in 77% of the PCOS patients with AN, while none of the PCOS patients were found to be diabetic among those without AN. A family history of DM in the first degree relatives was present in all the patients with AN. The results were analyzed by the Mann Whitney U test for the continuous data and by the Chi square test for the categorical data.

Conclusion: The PCOS patients who had a family history of diabetes and obesity with a body mass index of more than 30 kg/m^2 and a waist circumference of $\geq$ 90 cm were more likely to develop AN, which is a marker of hyperinsulinaemia and insulin resistance. Identifying such PCOS patients will stimulate the discussions of the lifestyle modifications in the primary care setting.

Key Words: Acanthosis nigricans, Diabetes mellitus, Polycystic ovary syndrome

BACKGROUND

The Diabetes Prevention Program study demonstrated that lifestyle interventions could prevent or delay the onset of Type 2 Diabetes Mellitus (T2DM) by as much as 58% [1]. Acanthosis nigricans is most commonly associated with the disorders which are associated with insulin resistance, which include obesity, T2DM, and Polycystic Ovary Syndrome (PCOS) [2]. Identification of the individual risk factor for the metabolic syndrome in PCOS, is an essential step in designing and implementing intervention programmes. Acanthosis Nigricans (AN) is characterized by thickening and darkening of the upper layers of the skin, which results in a velvety appearance. The typical areas which are involved are the posterior neck and the axilla. AN is a readily apparent and a rapidly identifiable physical examination marker, which identifies the patients who are at an increased risk for T2DM [3]. The incidence and the prevalence of AN in the general population is not known [4]. There is no epidemiological data to establish the prevalence of AN in PCOS and its correlation with diabetes and the body mass in our population.

METHOD

A prospective longitudinal study in the patients with PCOS, who attended the Department of Medicine, Kasturba Medical College Hospital, Attavar, Mangalore, India, between December 2008 to April 2010, was carried out, after taking approval from the institutional ethics committee.

A total of 119 female patients with PCOS were included in the study. A complete history was taken, along with the demographic data of the patients. The women with a confirmed diagnosis of PCOS, who were aged between 15-35 years, were selected. The women with a history of the intake of oral contraceptive pills or other hormonal preparations, anorexients, appetite stimulants and corticosteroids were excluded from the study. The diagnosis of PCOS was done by the Rotterdam criteria 2003, on the demonstration of two out of three of the following criteria [5]: 1) Oligomenorrhoea and/or Amenorrhoea; 2) Excess androgen activity – acne, hirsutism, infertility, high testosterone and an altered LH/FSH ratio; and 3) Polycystic ovary – More than or equal to 12 follicles on ultrasound examination. 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 $\geq$126mg/dL and a PPBS value of $\geq$ 200mg/dL were identified as diabetics. The diagnosis of AN was done clinically by a certified physician. The classification of body weight, depending on the BMI, was done as per the international classification [6].

RESULTS

A total of 119 patients with PCOS, who attended the Medicine Department during December 2008 to April 2010, were selected for the study. 66 of the PCOS patients had AN and 53 patients did not have AN.

	PCOS with AN	PCOS without AN	P
Age (Years)	28 ±5	25± 5	ns
BMI(Kg/m²)	30±6	25±5	0.001†
Waist (cm)	92±8	83±10	0.020*
Diabetes mellitus (%)	77	0	
Family History of DM in first degree relative (%)	100	77	

[Table/Fig-1]: Demographic data of the study sample

Values expressed as mean±SD. Categorical data were expressed as percentage. Mann Whitney U test applied for continuous data. *P≤0.05considered significant; †P≤0.001 highly significant;AN=Acanthosisnigricans; ns=not significant

There was no significant difference in the mean age among the PCOS patients. The BMI and the waist circumference were significantly higher in the PCOS patients with AN. T2DM was observed in 77% of the PCOS patients with AN, while none of the PCOS patients without AN were found to be diabetic. A family history of DM in the first degree relatives was present in all the patients with AN and in 77% of the patients without AN [Table/Fig-1].

BMI(Kg/m²)	AN(n=66)	NAN(n=53)	P
22.9 and less	8 (12%)	19 (36%)	0.0021*
23-24.9	5 (8%)	10 (19%)	0.0651
25 and above	15 (23%)	14 (26%)	0.6414
30 and above	38 (58%)	10 (19%)	0.0001*

[Table/Fig-2]: Distribution of Acanthosis Nigricans in different classes of BMI among PCOS patients

119: Obese PCOS = 92 (77%); 66(56%) were AN+; 52 (44%) NIDDM and all had AN & remaining 67 non diabetic; AN=AcanthosisNigricans;NAN= without AcanthosisNigricans, n = total number.Values are expressed as percentage in parenthesis. Chi-square test was used to find out statistical significance of differences in proportions.*P≤0.0001 considered highly significant.

In [Table/Fig-2], it can be seen that 36% 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 77% of the PCOS patients. AN was observed in 56% of the PCOS patients. This study showed that 58% of the patients had a BMI of more than 30kg/m² as compared to 19% of the patients who did not have AN. This was statistically significant.

Waist Circumference	AN(n=54)	NAN(n=44)	P
80-89.9	27 (50%)	36(82%)	0.0005*
≥90	27(50%)	8(18%)	0.0005*

[Table/Fig-3]: Distribution of AcanthosisNigricans among PCOS patients with respect to waist circumference

AN=AcanthosisNigricans; NAN=without AcanthosisNigricans, n=total number. Values are expressed as percentage in parenthesis. Chi-square test was used to find out statistical significance of differences in proportions. * P≤ 0.01 considered highly significant.

The results of [Table/Fig-3] show the occurrence of AN among the PCOS patients with respect to the waist circumference. AN was more in the patients with a waist circumference of ≥ 90 cm and it was lesser in the patients with a waist circumference of less than 90 cm as compared to the PCOS patients without AN.

DISCUSSION

PCOS is a common endocrine disorder in women of the childbearing age (15-20%). [7] It is characterized by obesity and insulin resistance. In 2000, a multicentric study which involved 6 urban cities in India (Chennai, Bangalore, Hyderabad, Mumbai, Calcutta and New Delhi), which was done among patients of the age group of 20-40 years, indicated that the prevalence rate of obesity was 31% in the general population [8]. The prevalence of obesity in the Indian PCOS population is 37.5% [9]. Similarly, in the present study, 92% of the PCOS patients were obese, which indicated a higher prevalence of obesity among the PCOS patients as compared to that in the general population.

In this study, it was found that among the obese patients, 58% among the AN patients and 19% among the non Acanthosis patients had a BMI of more than 30kg/m² [2.6]. 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 DM [10]. The waist circumference which indicates central obesity was higher in both the groups of patients with or without AN, but it was significantly higher in the patients with AN as compared to that in the patients without AN. The recommended waist circumference cutoff for Asian females is 80 cm. [Table/Fig-3] depicts a significantly increased occurrence of AN in the patients with a waist circumference of equal to or above 90 cm and a decreased occurrence in the patients with a waist circumference of less than 90 cm as compared to those in the PCOS patients without AN. So, those patients with a BMI of more than or equal to 30kg/m² and with a waist circumference of more than or equal to 90cm were more likely to develop AN, a marker of the insulin resistance. In a similar study, it was concluded that the elevated levels of the indexes that correlated with the degree of insulin resistance, such as the beta cell function index (HOMA-β) or the insulin level, were seen more often among the obese women with a BMI of >30 kg/m², among the polycystic ovaries patients [11].

The prevalence of AN in the general population in India varies from 7% to 30-40% [12]. Its 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 patients [13]. Similarly, in our study, the prevalence of AN was 56%, which was significantly higher as compared to its occurrence in the general population.

A national survey on diabetes and IGT which was conducted in 2000 in India, showed a 13.1% prevalence of IGT and a 5% prevalence of diabetes in the younger age group (20-40yrs) of the general population [8]. Obesity is a known risk factor for the development of insulin resistance and DM [14,15]. The PCOS women were at increased risk for IGT and T2DM in their younger ages. In our study, 77% of the obese patients also had T2DM 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 studies [16]. All the patients with AN had a history of T2DM in the first degree relatives and 77% among the patients without AN had a history of DM running in their first degree relatives. However, none of the patients had DM among those who did not have AN. The results of our study wassimilar to earlier studies. In a similar

study which was done in Brazil, all the patients were obese and the frequencies of diabetes mellitus (5.8%) and impaired glucose tolerance (12.6%) tended to be higher in the AN group [17]. In another study, a high BMI was significantly associated with the prevalence of T2DM and a significant number of patients with T2DM had AN [3]. These studies further confirm that the presence of AN among the PCOS cases with a high BMI indicates the risk for the development of insulin resistance and T2DM.

CONCLUSION

AN offers an intriguing possibility for encouraging lifestyle changes. Among the populations of the patients who have a family history of diabetes and are obese with a body mass index of more than 30 kg/m^2, with a waist circumference of 90cm and above, a readily apparent and a rapidly identifiable physical examination marker such as AN, can identify the patients with an increased risk for T2DM among the PCOS patients. This might help in stimulating discussions on lifestyle modifications in the primary care setting.

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