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CLINICO-DEMOGRAPHIC STUDY OF PATIENTS WITH ACANTHOSIS NIGRICANS

Dermatology

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ABSTRACT

Introduction- Acanthosis Nigricans (AN) is a fairly common skin pigmentary disorder .AN is characterized by dark, coarse and thickened skin with a velvety texture, being symmetrically distributed on the neck, the axillae, antecubital and popliteal fossae, and groin folds **Aim -** We have done this to study the prevalence, clinico-demographic and etiological profile of patients presenting with AN and to draw relations if any, with Coronary heart disease (CHD). **Materials and methods-** It was an observational, descriptive, institution based cross-sectional study and was conducted over a period of 18 months at the out patient department (OPD) of Dermatology, Venereology and Leprosy of A tertiary care hospital in Eastern part of India, Anattempt was made to detect etiological factor of the disease by noting the temporal association between the disease and any systemic associations with special attention to CHD. **Results-** Majority of our patients had high BMI(69%). Six patients had systolic hypertension(RR- 11.5000 and p was .0002) and diastolic hypertension in 12 patients (RR- 5.7500, p value- P<0.0001). So patients with AN, who have high BMI are more prone to develop hypertension, the most important criteria for Coronary Heart Disease. **Conclusion-** In AN , high BMI high triglycerides , high total cholesterol was significantly associated with systolic hypertension, but there is no significant association of LDL with any of systolic or diastolic hypertension.

KEYWORDS

Acanthosis nigricans, metabolic syndrome, risk factor, coronary heart diseases.

INTRODUCTION-

Acanthosis Nigricans(AN) is a fairly common skin pigmentary disorder. AN is characterized by dark, coarse and thickened skin with a velvety texture, being symmetrically distributed on the neck, the axillae, antecubital and popliteal fossae, and groin folds. Different varieties of AN include benign, obesity associated, acral, syndromic, malignant, unilateral, medication-induced and mixed AN[1]. Diagnosis of AN is largely clinical with histopathology needed only for confirmation. Early recognition of these conditions is essential for prevention of disease progression. Obesity is closely associated with AN and more than half of them are adults. We had embarked on this study to evaluate in a group of patients,the clinical and demographic features of AN and to find out its association with Coronary Heart Diseases(CHD), the most common epidemic which has significant public health influence.

AIMS AND OBJECTIVES-

To study the prevalence, clinico-demographic and etiological profile of patients presenting with AN and to draw relations if any, with Coronary heart disease(CHD).

MATERIALS AND METHODS-

An observational, descriptive, institution based cross-sectional study was conducted over a period of 18 months at the out patient department (OPD) of Dermatology,Venereology and Leprosy of A tertiary care hospital in Eastern part of India, that catering a very large geographic area. Patients of all ages and both sex presenting with AN were included in the study.

The demographic profile was recorded. Thorough clinical examination of the patients regarding morphology and the distribution of the lesion was performed. An attempt was made to detect etiological factor of the disease by noting the temporal association between the disease and any systemic associations with special attention to CHD.

We had followed the Asian standards for anthropometric and biochemical criterias of Metabolic Syndrome[2]. Those criteria's as - Normal BMI: 18.0-22.9 kg/m ^{2}, Overweight: 23.0-24.9 kg/m ^{2}, Obesity:>25 kg/m ^{2}. Dysglycemia if Fasting blood glucose level ≥100mg/dl, Hypertension- Systolic ≥130/ Diastolic ≥85mm Hg, High triglycerides≥150 mg/dl; LDL- 129 mg/dl is near optimal, and above 130 mg/dl is high. Total cholesterol is normal when it is ≤200 mg/dl, and high when >200 mg/dl, Fasting Insulin normal <25IU, high ≥25IU.

Statistics And Results——

Total number of 100 patient of AN attended during the abovementioned period with estimated prevalence was 0.831 per 1000population. Age ranged from 1 years to 60 years; the mean age being 21.33±10.99 years. Demographic profile of the study population given in **Table 1**.

Table 1- Demographic Profile

		Total=100	P value
AGE	Mean±SD	21.33±10.99	
	Median	17	
Sex (M:F)		36:64	0.0069
Residence	Urban:Rural	71:29	<0.0001
Income	APL:BPL	88:12	<0.0001
Education	Illiterate:literate	1:99	<0.0001
Religion	Hindu:Muslim	77:23	<0.0001
Occupation	Unemployed:Employed	79:21	<0.0001

Neck was the commonest site involved (41 % of patients) .

Figure 1—AN involving lateral part of neck of a 14 years male patient.

Other sites are depicted in **Table 2**. A comparative data regarding duration and BMI with different site involvement is given in **Table- 2**. Associations, noted with AN as, Alopecia(17%) ,

Figure 2: AN affected left aspect of axilla in a 15 years male.

Figure 3: AN affected right aspect of antecubital fossa in a 13 years male.

Figure 4: AN affected right side of cheek in a 37 years female Hirsuitism (34%),Skin Tags(30%), Dermatoses Papulosa Nigra (43%) and Acne Vulgaris(45%)(**Table 3**).

Figure 5: AN affected acral part in a 45 years man.

Table 2- Relation between duration, BMI with different involvement site.

Paraneters		ANNeck (n=41%)	AN Neck+Axil la (n=26%)	AN NECK+AXIL LA+ ACFOSSA (n=14%)	AN NECK+ ACRAL (n=19%)	Total (N=100)
Duration of Illness (mon th)	Mean±SD	33.04±40.62	26.96±22.82	22±14.84	31.05±27.90	29.54±31.36
	Median,	24	24	24	24	24
	IQR	12-36	12-36	12-24	12-36	12-36
Weight (kg)	Mean±SD	67.90±16.25	69.11±18.01	60.07±11.88	56-70	66.01±15.65
	Median	65	70	60	158.73±9.87	65
	IQR	59-75	52-84	52-70		55-74
Height (cm)	Mean±SD	155.34±12.56	148.69±17.17	147.14±11.81		153.11±13.87
	Median,	154,	151.50,	150,	156,	153
	IQR	150-160	146-160	135-156	152-165	148-160
BMI	Mean±SD	28.10±5.20	31.10±4.96	27.50±4.96	24.39±4.27	28.09±5.36
	Median,	28.64	31.08,	27.27,	23.46,	27.95
	IQR	24-30	28- 36	24-29	21-26	24-31

The biochemical parameters in AN patients were as in **Table 4**.

Table- 3- Associations noted between AN and other disorders .

NAME OF DISEASE	NUMBER OFPATIENT	PERCENTAGE
Androgenetic Alopecia	17	17%
Hirsutism	34	34%
Skin tag	30	30%
DPN	43	43%
Acne	45	45%

Table 4- The biochemical parameters in AN

		AN Neck (n=41)	AN Neck+Axilla (n=26)	AN Neck+Axilla+ AnteCubital Fossa(n=14)	AN Neck+Acral (n=19)	Total (N=100)
FBS	Mean±SD,	101.21±26.27	97.65±23.89	86.92±9.90	93.68±7.21	96.72±21. 73 73
	Median,	94	93.50	82.50	96, 89	93
	IQR	89-102.75	83-102	81-92	75-98	86-100
Total Cholesterol	Mean±SD	171.82±41.77	170.96±30.13	169.82±26.51	165.89±35.99	170±35.59
	Median,	161	177	165.50	155	163
	IQR	147-193	148-184	154-190	142-187	147-189
TSH	Mean±SD	3.59±2.74	2.88±1.79	3.73±3.30	5.10±5.38	3.69±3.33
	Median	2.98	2.70	2.48	2.88 7.53	2.82
	IQR	1.79-4.11	1.79-3.11	1.78-6.23	2.39-7.53	1.84-4.14
TG	Mean±SD	154.75±65.99	139±51.76	157±76.05	133.14±55.17	147.10±61.95
	Median,	141	131	142.50	122	131.50
	IQR	98-206	101-168	100-201	91-186	98-199
LDL	Mean±SD	92.73±21.16	97.23±14.59	96.38±19.47	97.02±24.18	96.07±21.07
	Median,	90	97.5	96.5	91	94
	IQR	78-104	93-104	79-107	83-102	81-104
Fasting Insulin Level	Mean±SD	18.76±9.91	18.49±9.01	17.59±8.45	16.97±8.22	28.19±99.68
	Median	18.50	19.38	16.96	19.24	19.13
	IQR	11.17-25.93	10.87-22.62	10.22-23.30	8.99-22.26	11.13-24.02

We have devided BMI, FBS, fasting Insulin, Total cholesterol, triglyceride and LDL value According to the Asian standard.After analysing the various parameters with systolic and diastolic hypertension , it was noticed very high RR (**Table-5**), that carries the significance that in patients with AN, presence of these factors carries a significant risk for development of CHD.

DISCUSSION—

Metabolic syndrome is defined as a group of disorders that includes, in addition to obesity, insulin resistance, dyslipidemia, arterial hypertension and other metabolic disorders associated with cardiovascular disease[3,4].Individual factors that make up metabolic syndrome pose cardiovascular risks, and the syndrome is nothing but the sum of these. Although the classification of metabolic syndrome is controversial, cardio-metabolic risk factors are known to exist since paediatric age[3,4,5,6] . AN is among the most common dermatologic manifestations of obesity and hyperinsulinism.

Hyperinsulinemia causes AN. Insulin resistance is thought to be a primary etiological factor in the development of cardiac dysfunction, higher prevalence being reported in non-ischemic heart failure population. It predates the development of cardiovascular disease and independently defines a worse prognosis. Reduction in endothelial function may be a link between Insulin Resistance(IR) and decline in cardiovascular performance. IR may be linked to endothelial dysfunction by the number of mechanisms such as disturbance in subcellular signaling pathway and PI-3-kinase/Akt pathway [7].

Acanthosis nigricans patients have hyperinsulinemia and may be at greater risk of atherosclerotic cardiovascular disease [8].

In our study ,we took a cohort of Acanthosis nigricans patients. We wanted to draw corelation by calculating Relative risk in those patients who has one factor of metabolic syndrome with those who have hypertension – systolic or diastolic.

Majority of our patients had high BMI(69%). Six patients had systolic hypertension(RR- 11.5000 and *p* was .0002) and diastolic hypertension in 12 patients (RR- 5.7500, *p* value- P<0.0001). So patients with AN, who have high BMI are more prone to develop hypertension, the most important criteria for Coronary Heart Disease. Inother study, though only within

Table 5 -Relative Risk of Various Parameters With Blood Pressure

Category	According To The Asian Standard								
			SYST HYP	RR	P		DIAST HYP	RR	P
BMI	High	69	6	11.5000	<0.0001	69	12	5.7500	P<0.0001
	Normal	31	94			31	88		
FBS	High	26	6	4.3333	P < 0.0001	26	12	2.1667	P<0.0154
	Normal	74	94			74	88		
Fasting Insulin	High	20	6	3.3333	P=0.0066	20	12	1.6667	P<0.1292
	Normal	80	94			80	88		
Total Cholesterol	High	16	6	2.6667	P<0.0320	16	12	1.3333	P<0.4174
	Normal	84	94			84	88		
Triglycerides	High	35	6	5.833	P<0.0001	35	12	2.9167	P<0.0004
	Normal	65	94			65	88		
LDL	High	8	6	1.3333	P<0.5810	08	12	0.6667	P<0.3501
	Normal	92	94			92	88		

children and adolescent had similar result with Acanthosis Nigricans. Acanthosis nigricans in overweight and obese children and adolescents is associated with elevation of bodyfat, blood pressure, insulin and homeostasis model assessment index, indicating that it is a clinical marker associated with the metabolic syndrome[4].

Fasting Insulin was high in 20% patients in our study. The RR of developing Systolic hypertension in AN patients with raised Fasting Insulin was 3.3333(*p* value=0.0066). The RR for Diastolic hypertension in the same group of patients was 1.6667(*p*value <1292). Our study supports other study. It was noticed that, Systolic blood pressure and waist circumference were significantly higher in Group 2(high BMI) in paediatric age group patients in Indian context[6].

Overweight is associated with increased rates of hypertension (HTN) and AN, a known risk factor for cardiovascular diseases. Blood pressure was found to be associated with high BMI in the present study, such that patients who were overweight had higher mean systolic and diastolic blood pressures compared to those who were not overweight. In a study to examine the complex causal relationships among AN, obesity, and IR in Mexican Americans (MAs) it has been seen that the occurrence of AN increased by obesity status: normal weight (11%), overweight (53%), and obese (65%); by prediabetes status (47%); and by MS status (67%), respectively . For example, based on odds ratios (ORs), children with AN are approximately 9/10 times more likely to be obese/overweight, 6 times more likely to have MS, and 2 times more likely to have prediabetes[9].

Triglycerides came as significant association in AN patients who developed Systolic and Diastolic hypertension, total cholesterol was significantly associated with systolic hypertension, and LDL was not in significant association with any of systolic or diastolic hypertension. These findings were in support of previous study [6].In a study on adult female with AN[10], systolic blood pressure, total cholesterol (mmol/l), triglycerides (mmol/l) and uric acid (mmol/l) levels were statistically significantly higher in diabetic women in acanthosis groups, though relative risk of developing hypertension was not assessed in any study. But larger epidemiologic study is important before drawing inference about all these factors

CONCLUSION-

So we can conclude that, neck is the commonest site, acne is the commonest association, and Family history of AN is very common. About the etiological association with other diseases, obesity and hyper-triglyceridemia were mostly found. Patients with AN, who have high BMI are more prone to develop hypertension . Triglycerides came as significant association in AN patients who developed Systolic and Diastolic hypertension, total cholesterol was significantly associated with systolic hypertension, but there is no significant association of LDL with any of systolic or diastolic hypertension. We can draw inference , high BMI, Triglycerides and total cholesterol as risk factor in AN patients to develop CHD.

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Conflict of Interest -The authors declare no conficts of interest.

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