

Prevalence of acanthosis nigricans and its association with physical activity in adolescents – School-based analytical cross-sectional study from Kochi, Kerala

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ABSTRACT

Introduction: Acanthosis nigricans (AN) is a brown to black, poorly defined velvety hyperpigmentation of the skin. It is a predisposition factor for Type 2 diabetes, malignancies and various endocrinopathies. The available data regarding AN from Kerala is limited. Our study aims to estimate the prevalence of AN and to examine its association with physical activity among the adolescents of age 13–14 years. **Methodology:** This analytical cross-sectional study was conducted in two grades of a school in Ernakulam district between June and December 2018 among 400 adolescents of age 13–14 years. The study proforma and the Physical activity questionnaire, Adolescents (PAQ-Adolescents), were self-administered to the students and the data were collected. The principal investigator verified the presence of AN by observation in the neck, elbow and knuckles and recorded in the study proforma. Statistical analysis of the data collected was done using SPSS Software program (version 21). **Results:** The mean age of the group was found to be 13.31 ± 0.46 years. The prevalence of AN was 14.5% in the study population. AN was most prevalent among obese adolescents (61.54%), adolescents with low exercise rate (23.94%), having family history of diabetes (21.18%), family history of hypertension (21.86%) and family history of both diabetes and hypertension (26.32%). The risk factors such as obesity, diabetes, hypertension, family history of diabetes, family history of hypertension and family history of both diabetes and hypertension had a positive association with AN had a negative association with physical activity with $p=0.0001$. In adolescents with increased exercise rate, there were no reported cases of AN. **Conclusion:** The results of our study show that there is a strong association between AN and children with obesity, family history of diabetes mellitus, hypertension and low physical activity. Regular adequate physical activity can prevent the onset of AN and thereby reduce the early onset of diabetes, metabolic syndrome, polycystic ovarian syndrome, coronary artery diseases and certain types of malignancies.

Keywords: Acanthosis nigricans, adolescents, physical activity, risk factors

Introduction

According to WHO, 40.5 million or 71% of global deaths in 2016 were due to noncommunicable diseases (NCDs).^[1] In India, adolescents having NCDs are on the rise^[2] NCDs such as obesity, diabetes mellitus (DM), hypertension, coronary

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artery disease and stroke in the later part of life have been related to the presence of risk factors in childhood and adolescence.^[3] Identifying the risk factors for NCD in the early years of life such as childhood/adolescence will certainly help to prevent the occurrence of these chronic diseases in future.^[4] Evidence shows that certain cutaneous markers can predict the chances of getting NCDs in the later years of life.^[5] Acanthosis nigricans (AN) is the widely used cutaneous marker to identify the risk factors of NCD, namely, metabolic syndrome comprising of obesity, DM, hypertension and dyslipidemia.

AN is a dermatosis characterized by velvety, papillomatous, brownish-black, hyperkeratotic plaques, typically of the intertriginous surfaces and neck.^[5] AN previously was thought to be associated with polycystic ovarian disease, but later it was found to be closely related to Insulin resistance.^[6] The pathophysiology of AN may be that insulin, when present in supraphysiological concentrations, acts on skin keratinocytes, via the insulin-like growth factor (IGF-1) receptor, to cause keratinocyte proliferation.^[7] AN is considered as one of the noninvasive methods to determine those at increased risk of metabolic abnormalities especially those in the childhood and adolescent age group.^[8] AN in children and adolescents is considered as a strong predictor for occurrence of DM. Early identification of risk factor for DM can prevent the burden of DM among population. In low- and medium-income countries where resources are low and treatment cost is high, identifying children and adolescents at risk will be a useful measure to prevent DM. Moreover, it provides enormous opportunity to implement preventive strategies among such high-risk population.^[7]

Physical activity has been proven to be a preventive strategy against development of insulin resistance associated with childhood.^[9] This relation between physical activity and AN has been found to be of significant association in many populations and is more seen among obese children with less physical activity than with regular physical active lifestyle.^[10] It was observed that obese children and adolescents with AN had high prevalence of hyperinsulinemia. Physical activity has been found to be protective against hyperinsulinemia irrespective of whether the children were having obesity or AN.^[6]

The prevalence of AN was found to be 15.5% of those in the age group of 12–19 in a study done by Das *et al.*^[13] In that study, AN was seen in 42% of obese children. In a study conducted in North Kerala, the prevalence of AN among 507 school children between age group of 10 and 18 was found to be 39.5%, and the association between AN and insulin resistance was found to be statistically significant. When AN was combined with high body mass index (BMI), the incidence of insulin resistance was found to be 80%.^[14]

Literature about the prevalence of AN among children and adolescents among south Indian population is limited. Hence, this study was undertaken with the following objectives.

Primary Objective: To estimate the prevalence of AN in high school adolescents of age 13–14 years.

Secondary Objectives: 1) To examine the association between AN and physical activity in the study participants.

2) To examine the association between risk factors and AN in the study participants.

3) To examine the association between BMI and AN in the study participants.

Materials and Methods

This analytical cross-sectional study was conducted in two grades of a high school (8th and 9th grade) at Ernakulam district between June and December 2018. The study duration was for a period of 7 months. The inclusion criteria were adolescents in the age group of 13–14 years, without any disability to do physical activity and able to comprehend in English and native (malayalam) language. All students studying in the two grades were consecutively enrolled for the study. A structured study proforma was used to collect the data.

The study proforma had questions regarding demographic details, risk factors, site of presence of AN. The physical activity details were collected using the Physical activity questionnaire – Adolescents (PAQ-Adolescents).^[15] Parental consent and child assent was taken before the data collection. Physical activity scoring criteria were: low physical activity – Mean score <2, Moderate physical activity – Mean Score 2–4.5, High physical activity – Mean score >4.5.

The principal investigator (PI) and the research personal measured the height and weight of the study participants. The PI examined the presence of AN in areas such as neck, elbow and knuckles by visual observation and recorded in the study proforma. The collected data were transferred to Microsoft excel and analysed using IBM Statistical Package for Social Science (SPSS version 21). The summary statistics for categorical variables are reported as frequency and percentage and continuous variables as mean (SD). Prevalence is reported as %. The association of the AN with level of physical activity is reported using Chi-square test. *P* value <0.05 is taken as statistically significant.

Ethical approval

The study got approval from the institutional ethics committee (IRB-AIMS-2017-125). Written informed consent was taken from parents of the participated children. Confidentiality of the study participants was maintained throughout the study.

Results

A total of 400 subjects were included in the study. The mean age of the study population was 13.31 ± 0.46 years. The proportion of males in the study population was 207 (51.7%). The urban

rural distribution was 343 (85.8%) and 57 (14.2%), respectively. The occurrence of AN was more in children coming from rural areas (22.8%). The distribution of risk factors were diabetes 2 (0.5%), hypertension 2 (0.5%), obesity 13 (3.3%), family history of diabetes 170 (42.5%), family history of hypertension 96 (24%) and family history of both diabetes and hypertension 57 (14.2%). AN was seen more in obese children (61.5%), children with family history of both hypertension and diabetes (26.3%), children with family history of hypertension (21.9%) and children with a family history of diabetes (21.2%). The details of the baseline characteristics with the distribution of AN in the study population are shown in Table 1.

The overall prevalence of AN was 14.5% ($n = 58$) in the study population. Neck was the site in which AN was most seen. The distribution of AN according to sites was neck ($n = 39$, 67.2%), elbow ($n = 25$, 43.1%) and Knuckles ($n = 15$, 25.9%).

The distribution of risk factors in those who had acanthosis was diabetes 2 (3.4%), hypertension 2 (3.4%), obesity 8 (13.8%), family history of diabetes 36 (62.1%) and family history of hypertension 21 (36.2%). Those who had a family history of diabetes showed a high prevalence of acanthosis. All risk factors had a positive association with acanthosis and were also statistically significant. The details are represented in Table 2.

Physical activity had a negative association with AN. As the grade of physical activity increased, the presence of acanthosis was declining. The negative association was statistically significant with $p=0.0001$. The details are represented in Table 3.

Discussion

AN usually presents as a thickened, dark, coarse skin with a texture that is velvety. The velvety texture is due to the papillomatous projections on the thickened skin. It is symmetrical distributed usually with common areas affected being neck, axilla followed by groin, and antecubital regions. Obesity has been identified as one of the most common cause for AN. In children, common occurrence of AN is the neck region followed by axillae.^[16]

Obesity in children is of high significance in public health because it tends to be carried on into adulthood.^[17-20] The ill-effects of obesity can be manifested at any stage of later life; thus, addressing the obesity at an early age is essential in preventing future chronic diseases.^[19] Obesity is commonly linked to physical inactivity.^[10] Hence, the rationale of linking physical activity with AN is relevant in this era, where the risk factors of metabolic diseases can be identified at an early stage and appropriate precautionary measures could be taken to prevent development of future illness.

The most striking observation obtained from this study is the association between obesity and AN, which was found to be highly significant. Although, the relation between AN and physical activity is complex, it has been found that adolescents

Table 1: Baseline characteristics and distribution of AN in the study participants

Variables	Frequency (%)	AN (n, %)
Demographic variables		
Females	193 (48.3)	23 (39.7)
Males	207 (51.7)	35 (60.3)
Rural	57 (14.2)	13 (22.8)
Urban	343 (85.3)	45 (13.1)
Risk factors		
Diabetes mellitus	2 (0.5)	2 (0.5)
Hypertension	2 (0.5)	2 (0.5)
Obesity	13 (3.3)	8 (61.5)
Family history of diabetes mellitus	170 (42.5)	36 (21.2)
Family history of hypertension	96 (24)	21 (21.9)
Family history of both diabetes and hypertension	57 (14.2)	15 (26.3)
Physical activity categories		
Low	188 (47.0)	45 (23.9)
Moderate	170 (42.5)	13 (7.6)
High	42 (10.5)	0 (0.0)

Table 2: Association of risk factors with acanthosis nigricans

Risk factors	Acanthosis nigricans		P
	Present	Absent	
Diabetes mellitus	2 (3.4)	0 (0.0)	0.021
Hypertension	2 (3.4)	0 (0.0)	0.021
Obesity	8 (13.8)	5 (1.5)	0.0001
Family history of DM	36 (62.1)	134 (39.2)	0.001
Family history of HTN	21 (36.2)	75 (21.9)	0.019
Family history of both DM and HTN	15 (25.9)	42 (12.3)	0.006

Table 3: Association of physical activity with acanthosis nigricans

Physical activity grades	Acanthosis nigricans		P
	Present	Absent	
Low	45 (23.9)	143 (76.0)	0.0001
Moderate	13 (7.6)	157 (92.4)	
High	0 (0.0)	42 (100)	

with insulin resistance tend to be obese. AN occurs more in adolescents with obesity who have low physical activity.^[10] The findings of the present study are in tune with the above findings observed among Mexican American children, where the association between obesity and AN was found to be significant.

AN occurs rarely as a paraneoplastic syndrome, but commonly associated with insulin resistance. The high circulating insulin could trigger insulin-like growth factor I (IGF-I), which can be direct or indirect. This explains the occurrence of in subjects with insulin resistance. Tyrosine kinase factor signalling has also been found to be associated with incidence of AN.^[21] This could explain the higher incidence of AN among those identified with DM.

In a nation-wide study conducted by Indian Council of Medical Research (ICMR), physical inactivity was present in 54.4% out of

14,227 subjects, which is alarming. Males were significantly more active than females. This rising trend was observed in developed nations too over the past decade.^[22] The present study shows similar findings as those by ICMR, wherein the occurrence of physical inactivity was 41.8%.

Prehypertension and hypertension were found to be highly associated with occurrence of AN among children and adolescents in a major cross-sectional study conducted among American Indians. It was also observed that as age progresses there can be clustering of risk factors for chronic life style diseases like diabetes.^[23] The findings of the present study correlate with that of observations made among children and adolescents among American Indians.

In a study conducted among children in Brazil, AN in obese and overweight children were significantly associated with elevated levels of insulin and hypertension.^[24] The same association was also found among 543 Chinese children who were obese, where the authors observed that obese Chinese children with AN are at a higher risk of having cardio metabolic comorbidities and insulin resistance.^[25] The observations made among Brazil and China which associate insulin resistance and risk of diabetes strike a chord with the present study, where subjects with diabetes were found to be more at risk of developing AN and the association was found to be statistically significant. The observations made among Brazilian children were similar to the findings of the present study, where subjects with hypertension were found to have AN.

Obesity is considered as a risk factor in the 21st century for numerous NCDs, and it affects multiple systems of the human body.^[11,26] AN, Type II DM and hypertension are all interlinked and shares a common genetic base as proposed by thrifty metabolism theory.^[7] However, this has been contradicted by thrifty phenotype hypothesis, where the authors gave more weightage to environmental rather than genetics for the development of DM.^[27] AN is closely associated with insulin resistance and obesity, and it has been found to be inversely associated with physical activity. The relationship between obesity, AN, insulin resistance and cardiometabolic risk factors is complex and has genetic as well as pleiotropic influences. AN can be thus considered as a compound marker for metabolic risk in children and adolescents.^[10,12] Similar observations supporting the above-mentioned association were found in the present study, where AN is significantly high in children with obesity and hypertension. Also, subjects with family history of diabetes were shown to have highly significant incidences of AN. These findings are concurrent with the theory that DM and hypertension could share a common genetic basis. In a study conducted in North India, AN and acrochordon were found to be more in subjects suffering from insulin resistance, but it was not found to be statistically significant, may be due to low sample size.^[28] AN though cannot be completely cured can be treated to a large extent. The prevalence of AN is increasing in different regions of the world in various ethnic groups. To get

more insights into its pathophysiology and effective treatment, long duration studies are a must in future.^[29]

The observation as obtained from this study that AN is rarely found or almost nil in adolescents with high physical activity is an encouraging finding, as it could prevent a huge burden of NCDs in the future generation. Childhood and adolescent obesity is usually carried forward as adult obesity is a matter of concern and should be seriously dealt with giving it due importance.^[17] In order to prevent the incidence of various chronic diseases, screening of adolescents and children with AN for such diseases and constant monitoring of BMI will be of huge value from the public health perspective.^[14] Early detection of AN in children by the primary care physicians can certainly prevent the occurrence of metabolic syndrome and related diseases in future for these children. This in turn would help to create a healthy population with healthy life style.

Conclusion

Our study results show that in the state of Kerala with high literacy, the primordial and primary preventive measures for life style diseases are only in the evolving phase. AN was seen more in adolescents with less physical activity than those with moderate to high physical activity. In children with high physical activity among the study participants, AN was totally absent. Studies have proved that AN in children undoubtedly can be considered as a biomarker for predicting occurrence of chronic diseases in future. There exist strong scientific evidences that AN can be reduced through enhancing the physical activity and modifying the diet during childhood and adolescence. School-based attempts to increase and sustain a moderate to high level of physical activity must be ensured to achieve a healthy population in the present and coming generation.

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Conflicts of interest

There are no conflicts of interest.

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