

Prevalence and risk factors associated with acanthosis nigricans in children

: A systematic review and meta-analysis

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Abstract

• Background

Acanthosis nigricans (AN) is characterised by pigmented velvety thickening of the intertriginous body regions.

• Methods

I performed a systematic review on the Acanthosis nigricans prevalence and risk factors associated with it in children.

• Results

Systematic review of 8 articles found a close relationship between AN in pediatric patients and endocrinopathies. This meta-analysis showed that the etiology of Insulin resistant ranges from:
□ Congenital. □ Acquired factors. Both genetic and environmental factors play significant roles. □ Fetal malnutrition /under nutrition. □ Insulin receptor defect to physiological conditions such as pregnancy, high fat diet, sedentary, life style have all been implicated. □ Hormonal disorders, such as pheochromocytoma, steroid overdose have been implicated by some researchers. □ In recent times, raised blood pressure and obesity and polycystic ovarian syndrome (PCOS) have been included. □ It is also associated with fatty liver.

• Conclusion

This systematic review and meta-analysis suggest that we need to perform skin inspection regularly for early identification of AN and any dermatological sign.

• Keywords

Prevalence-Acanthosis nigricans-Primary school-Children.

Introduction:

Acanthosis Nigricans (AN) is a dermatosis characterized by velvety, papillomatous, brownish-black, hyperkeratotic plaques, typically on the intertriginous surfaces and neck [1]. Histopathologic changes of AN consist of hyperkeratosis, acanthosis, and mild papillomatosis. The dermis is usually normal, but can present with elongated dermal projections, while the brownish color is due to the thickening of the stratum corneum; however, a silver nitrate stain can sometimes show melanin [2]. Acanthosis nigricans recognition should prompt the clinician to further evaluate the patient clinically to determine the underlying cause, which may be benign (obesity related, hereditary, endocrine or malignant). Its frequency is often underestimated being asymptomatic [3].

Acanthosis nigricans is a frequently seen in middle aged or elderly, but in the recent times, there has been an increase in the childhood cases [4]. Acanthosis nigricans has no known sex predilection. An Indian study showed that 77.8% were females and 22.2% were males [4].

This distribution pattern of AN with high frequency on the neck and axillae can be

caused by mechanical factors have an important role in proliferation of skin keratinocytes, their influence being integrated by complex cellular signaling.

Other areas that may be involved are conjunctiva, lips, eyelids, flexor and extensor surface of elbows and knees, knuckles, external genitalia, areolae, inner face of thighs and anus. In some cases, especially when associated with malignancies, AN may interest the mucosa of the oral cavity, esophagus, nose or larynx [5].

Acanthosis nigricans types included (obesity-associated acanthosis nigricans, syndromic acanthosis nigricans, malignant acanthosis nigricans, unilateral Acanthosis nigricans, acral acanthosis nigricans, drug-induced acanthosis nigricans and mixed acanthosis nigrican [6].

Obesity-associated AN consider the most frequent form, lesion severity being related with weight excess. Lesions are often slowly reversible after weight loss. It is more common in obese patients with insulin resistance [4]. Some skin conditions may be an indicator of the presence of type 2 Diabetes in children and adolescents, the most common of these is AN, it has been demonstrated as a reliable marker for insulin

resistance in children and adolescents with obesity [7].

Many studies showed a high proportion of depressive symptoms in obese patients with AN higher than that obese only [8]. There is no specific treatment for AN. Treatment is directed towards the specific symptoms that are apparent in each individual. It should be borne in mind that such treatment may require the coordinated efforts of a team of medical professionals aiming to Correcting the underlying disease improves the skin symptoms. Steps that may be taken, depending on what the disease is, include correcting hyperinsulinemia through diet and medication, with encouraging the loss of weight in those with obesity-associated AN, removing or treating a tumor, and discontinuing a medication that causes AN. The control of obesity contributes significantly to reversing the whole process [9].

Methods:

- **Literature search**

The articles reviewed were retrieved from searches conducted on the Web of Science database on October 2021. In the first search, the search criteria used were: document type ‘article’, search terms ‘acanthosis nigricans’ in the topic and ‘pathogenesis’ in the title. Additional searches using the following criteria—document type ‘article’ and either the

search terms ‘acanthosis nigricans’ and ‘predisposition’ in the topic or search terms ‘acanthosis risk factors’ in the topic—were also conducted. The aim of the present studies were to determine more prevalent skin diseases among the overweight and obese patients people and to examine if overweight and obesity are risk factors for skin diseases

- **Criteria for meta-analysis**

Studies were included in the meta-analysis if they satisfied the exclusion criterion included were: with any diseases other than dermatological origin.. Of 34 search results found, a total of 8 articles were chosen based on selection criteria.

Results

A total of 8 articles, were chosen from 34 results in searching the Prevalence and risk factors associated with acanthosis nigricans in children

1. All of studies found a significant association with acne alone or both acne and acne severity, but some studies found insignificant associations with acne severity alone.

The first article which carried out on 250 overweight or obese patients as a cases group and another 250 normal weight patients were included as a control group . most common skin diseases among cases were tinea pedis (41.2%), hair dandruff (26.8%), striae (68.4%), intertrigo (53.6%), skin tag (61.2%), planter hyperkeratosis (61.6%), and acanthosis nigricans (53.6%). Among the controls, the common skin diseases included: hair dandruff (28%), acne (14%), tinea pedis (18%), callosity (11.2%), striae (12.8%) and skin tag (15.6%). It was found that Odds ratio of the following diseases in

cases were; planter hyperkeratosis (42.9), intertrigo (16.9), striae (14.7), varicose vein (14.3), skin tag (8.5), psoriasis (4.03) and hirsutism (10).

The second one, malignant acanthosis nigricans in patients with cancer is poor prognosis, for it is usually a high-grade neoplasm associated to metastases. Malignant forms can be clinically indistinguishable from benign acanthosis nigricans, therefore, a good history taking is essential to investigate cases of rapid onset and a thorough physical examination is needed to evaluate the involvement of uncommon regions and extensive locations (11).

The 3rd article The participants were randomly selected from four different areas in Palestine. A total sample comprising 392 students. The results revealed that obesity prevalence was 3.3% and overweight was 13.8% among the students, with no significant association with gender, age, or area of living. Obesity and overweight were significantly associated with lower self-satisfaction ($P < 0.01$). (12).

The 4th article was cross sectional study with comparative group, total 162 age and sex matched subjects were divided into two groups of cases with acanthosis nigricans and comparative subjects without acanthosis nigricans. The severity acanthosis nigricans was assessed using the Burke's quantitative scale. Fasting blood sugar and fasting insulin levels were estimated to know the Homeostasis model assessment of insulin resistance (HOMA-IR) values. Data was analyzed by using appropriate statistical tests. Acanthosis nigricans was strongly associated with insulin resistance with significant odds ratio and statistical significant p value ($P <$

0.05). Acanthosis nigricans severity, neck severity and neck texture severity showed positive correlation with fasting serum insulin with statistically significant p value ($P < 0.05$). (13)

The 5th article, As a consequence of the ongoing pandemic of obesity, AN associated with obesity is the most common cause of AN, which is true even for the pediatric population. In a study of 234 Israeli children and adolescents who were obese, 81% were given the diagnosis of insulin resistance and 56.6% manifested AN. (14).

The 6th article, cross-sectional controlled study, we included men or women, with or without AN in the knuckles. In 149 cases with AN in the knuckles and 145 controls, fasting insulin was higher in cases, $P < .001$, respectively). Mean HOMA-IR index was also higher $P < .001$). A significant increase in fasting insulin and HOMA-IR values between and within BMI groups from normal through obese category was identified in controls and cases. (15).

The 7th article was about 88 obese patients treated in our department were selected for analysis. They were divided into simple obesity and obesity with acanthosis nigricans. A control group included 56 normal weight healthy volunteers. Result was the frequency of depressive symptoms was recorded as 67.2% in the AN group, 43.4% in the second group, and 3.6% in the third group ($P < 0.001$) (16).

The last article included in my study was weight children. Anthropometric body measurements, bio-specimen and biochemistry assays were done. Genotyping of rs9465871 (CDKAL1) was conducted, There is a significant risk association between CDKAL1-rs9465871 polymorphism and development

of T2DM in a subset of the Egyptian children (17)

Discussion

A total of 8 articles were chosen from 34 results in searching the Prevalence and risk factors associated with acanthosis nigricans in children. All of studies showed significant association of acanthosis nigricans cases with fasting insulin and HOMA-IR ,but no association with fasting blood sugar as compared to subjects without acanthosis nigricans, but some studies found insignificant associations with with fasting glucose alone.

Conclusion

In conclusion, this review summarizes the literature on acanthosis nigricans , this cross sectional study with comparative group acanthosis nigricans was found to be strongly associated with insulin resistance .Acanthosis nigricans severity grading, neck severity and neck texture showed positive correlation with fasting serum insulin with statistically significant p value ($P < 0.05$). The studies found considerable prevalence of obesity and overweight among adolescents living in different area, but there is no significant association between being obese or overweight with any of the socio demographic variables, — Further research using different study designs is recommended to examine obesity and its risk factors among other age groups in different areas.

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