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Acanthosis Nigricans in Obese Iraqi Children

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Abstract: Objectives: To study overweight and obese children and adolescents in Iraq whom presented with and without acanthosis nigricans

And the relationship between acanthosis nigricans with insulin resistance and cardiometabolic comorbidities

Research paradigm: The research employs a case series with use of cross-sectional analyses.

Patients: The main focus of the investigation are the demography of Iraq children. These children were studied from April 2021 through January,2025. The justification for their inclusion is the fact that they are found to be overweight and obese from one hospital.

Main measures: The demographic, acanthosis nigricans status, anthropometric data, and biochemical results were the main items of analyses.

Results: the study concentrated on a total of about 75 overweight and obese children in Iraq. Out of this number, 47 were boys representing (63%), Acanthosis nigricans (AN) was noticed in 41 of subjects (55%), and 23 that is (29%) got insulin resistance (IR). Adolescents of age between 12-18 years were more than children of 5-11 years of age to have obtained AN (25/40) that is, [62%] vs. 16/35 that is [46%]; P<0.001) as well as IR (15/40 [38%] vs. 9/35 [26%]; P=0.005). Compared with overweight children, those who obese were more likely to have AN (34/59 [60%] vs. 7/16 [43%]; P=0.006) and IR (21/59 [36%] vs. 3/16 [18%]; P=0.002). Children with AN showed significantly higher mean systolic blood pressure, fasting insulin, HOMA-IR, triglycerides, and ALT, as well as lower HDL cholesterol levels compared to those without AN (all P<0.05). They had IR (P<0.001), where hypertension is (P=0.021), while fatty liver is (P=0.001), and abnormal glucose homeostasis is (P=0.003).

Conclusion: the result of this study revealed that children and adolescents in Iraq with obesity and acanthosis nigricans obtain increased possibility of insulin resistance and cardiometabolic co-morbidities. AN is an essential clinical sign necessitating early evaluation to allow appropriate interventions..

Introduction

The world health organization confirmed obesity as one of the serious global pandemics in 1997 [1,2]. For several years, the occurrence of the two major issues overweight and obesity has substantially increased globally.

The obese and overweight children and adolescents have the possibility to develop hypertension, hyperinsulinemia and dyslipidemia. The grouping of these cardiometabolic risk issues in childhood usually continues through adulthood, which eventually increase the risk of serious disease later in life. Conversely, the effect of lifestyle modifications has been shown to prevent the onset of type 2 diabetes mellitus (T2DM) with significant effect [3 & 4]. One of the major preventive way of cardiometabolic complications is to identify the children at risk earlier.

Acanthosis nigricans (AN), a hyperpigmented, thickened, and velvety skin lesion are noticed on the nape of the neck or axilla. This serves as an early and easily method of identifying the clinical signs [5]. One of the prominent organizations is the American Diabetes Association, that observes AN as a possible risk of developing diabetes mellitus especially among overweight youth who progresses towards puberty, but some researchers argue that AN cannot be considered as an independent predictor of insulin resistance (IR) as long as elevated body mass index is found [6 & 7).

There are limited studies on the connection between AN, insulin resistance, and cardiometabolic co-morbidities in Iraqi children. This study therefore, aims to address this problem, with the main focus on the connection between AN, IR, and other cardiometabolic comorbidities [8,9].

Methods

This is a Case series study where cross-sectional analyses were also involved with the recruitment of overweight and obese children in Iraq. Their age was between 5-18 years. These groups of children went through obesity assessment procedure at one of the regional hospitals located in Iraq from April 2021 to January 2025. Other patients with underlying metabolic diseases which contribute to obesity were not included in the study. Similarly, those patients who are on medication were also excluded.

Anthropometric measurements and acanthosis nigricans (AN) status were documented. The study involved the collection of blood samples for purpose of biochemical analysis. The hepatic ultrasound scanning of patients with elevated alanine aminotransferase (ALT) levels were done. Height of these patients was measured with the use of an approved stadiometer as well as the weight was measured by electronic scale. In this study, the overweight and obese groups were defined as a body mass index (BMI) of between 85^{th} and 95^{th} percentiles, and above 95^{th} percentile respectively. The calculation of the BMI z-score was according to these age and sex of the children.

Likewise, Blood Pressure (BP) was assessed with the use of an approved oscillometric device, after the children were relaxed during the daytime. The two measurement results were recorded and average was obtained. In this sense, the term hypertension was viewed as a diastolic or systolic BP z-score at or above the percentile of 95^{th} in relation to gender and age.

Diagnosis of acanthosis nigricans was made clinically by single dermatologist. Quantitative scoring was not performed, as the utility of specific scales in predicting insulin resistance remains debated.

A blood samples were obtained after overnight fasting for insulin, lipid profile, liver enzyme analysis and plasma glucose. Similarly, a standard procedure for oral glucose tolerance test (OGTT) was also carried out. The resistance of insulin was conducted through the use of homeostasis model assessment of insulin resistance (HOMA-IR). A HOMA-IR value of ≥ 4 was measured revealing the insulin resistance.

Glucose irregularities were defined based on the criteria approved by the World Health Organization. Abnormal glucose homeostasis involved the combination of impaired fasting glucose, impaired glucose tolerance based on two-hour plasma glucose or fasting glucose during the OGTT.

Likewise, fatty liver was diagnosed by ultrasound and affirmed based on the definition of non-alcoholic fatty liver disease (NAFLD) that is related to the Asia Pacific domain

Results

As stated, the study engaged 75 obese and overweight children in Iraq. Their mean ± standard deviation age was 11.5 ± 3.0 years, 47 (63%) were males. The result indicated that most of them were obese 59 (79%) and 16 (21%) were found to be overweight. Acanthosis nigricans (AN) was found in 41 which represents (55%) of the participants and 23 (29%) confirmed to have insulin resistance. demographic and clinical information are presented in the following table.

Table 1. main features of 75 children

Characteristics	No. (%) of patients
Age (years)	
All	75 [11.5 ± 3]
5–11 years	35 (47%)
12–18 years	40 (53%)
Sex	
Male	47 (63%)
Female	28 (37%)
BMI category	
Overweight (90–97%)	16 (21%)
Obese (>97%)	59 (79%)
Acanthosis nigricans	
Present	41 (55%)
Absent	34 (45%)
Insulin resistance (HOMA-IR)	
HOMA-IR <4	52 (71%)
HOMA-IR ≥4	23 (29%)

Table 2. Assessment of acanthosis nigricans and insulin resistance in sub-groups

Subgroup	AN Present	P value	Insulin Resistance (HOMA-IR ≥4)	P value
Age (years)				
5–11 (n = 35)	16 (46%)	<0.001	9 (26%)	0.005
12–18 (n = 40)	25 (62%)		15 (38%)	
BMI category				
Overweight (n = 16)	7 (43%)	0.006	3 (18%)	0.002
Obese (n = 59)	34 (60%)		21 (36%)	

Basic Abbreviations: AN = acanthosis nigricans; BMI = body mass index; HOMA-IR = homeostasis model of assessment–insulin resistance

Table 2 shows subgroup comparisons. Adolescents (12–18 years) were more likely than younger children (5–11 years) to have AN (25/40 [62%] vs. 16/35 [46%]; P<0.001) and IR (15/40 [38%] vs. 9/35 [26%]; P=0.005). A comparison of children with obesity with overweight participants also show a higher prevalence of AN (34/59 [60%] vs. 7/16 [43%]; P=0.006) and IR (21/59 [36%] vs. 3/16 [18%]; P=0.002).

Table 3. Evaluations among the groups with and without acanthosis nigricans

Variable	With AN (n = 41)	Without AN (n = 34)	P value
Age (years)	12.4 ± 2.5	11.5 ± 3.0	0.001
Sex (M/F)	28 / 13	19 / 15	0.227
Body weight (kg)	70.8 (57.9–83.7)	59.0 (46.1–71.9)	<0.001
Height (cm)	156.4 (146.9–164.0)	149.8 (137.5–161.0)	<0.001
BMI (kg/m²)	28.8 (26.1–31.7)	26.0 (24.1–28.5)	<0.001
BMI z-score	2.3 ± 0.4	2.2 ± 0.4	<0.001
Systolic BP (mmHg)	119.5 ± 9.3	116.2 ± 9.8	<0.001
Systolic BP z-score	1.1 ± 0.9	1.0 ± 0.9	0.175
Diastolic BP (mmHg)	61.6 ± 7.1	60.7 ± 7.4	0.174
Diastolic BP z-score	–0.3 ± 0.9	–0.3 ± 0.8	0.774
Fasting glucose (mmol/L)	4.9 ± 0.5	4.9 ± 0.4	0.598
2h post-OGTT glucose (mmol/L)	6.4 ± 1.6	6.1 ± 1.1	0.021
Fasting insulin (µU/mL)	16.8 (11.2–25.3)	11.8 (8.4–16.2)	<0.001
HOMA-IR	3.6 (2.5–5.3)	2.6 (1.8–3.6)	<0.001
Total cholesterol (mmol/L)	4.4 (4.0–5.1)	4.5 (4.0–5.0)	0.913
LDL (mmol/L)	2.6 (2.1–3.1)	2.5 (2.1–3.0)	0.535
HDL (mmol/L)	1.2 (1.1–1.4)	1.4 (1.2–1.6)	<0.001
Triglycerides (mmol/L)	1.3 (1.0–1.8)	1.1 (0.9–1.6)	<0.001
ALT (U/L)	24.0 (17.0–41.0)	20.0 (15.0–32.0)	0.002
Insulin resistance (HOMA ≥4)	18 (44%)	5 (15%)	<0.001
Hypertension	10 (24%)	3 (9%)	0.021
Fatty liver	12 (29%)	2 (6%)	0.001
Abnormal glucose homeostasis	8 (20%)	2 (6%)	0.003

Table 3 above shows comparison between children with or without AN and some of them AN were basically older (12.4 ± 2.5 vs. 11.5 ± 3.0 years; P=0.001), and as well, had essential high body weight, BMI, height, BMI z-score, fasting insulin, HOMA-IR, systolic, blood pressure, atriglycerides, as well as ALT levels, and, higher 2-hour post-OGTT glucose levels. However, they had low HDL cholesterol levels (all P<0.05). But, when regulated as z-scores, systolic and diastolic blood pressure remain unchanged significantly between the two different categories.

Children with AN were more likely to have IR (44% vs. 15%; P<0.001), hypertension (24% vs. 9%; P=0.021), fatty liver (29% with 6%; P=0.001), and abnormal glucose homeostasis was (20% with 6%; P=0.003).

Table 4. link between clinical and laboratory data and insulin resistance (HOMA-IR ≥4) based on multivariate analysis

Variable	IR Present (n = 23)	IR Absent (n = 52)	P value
Age (years)	12.6 ± 2.3	11.7 ± 2.9	0.002
BMI z-score	2.4 ± 0.4	2.2 ± 0.3	<0.001
Acanthosis nigricans (Present/Absent)	18 / 5	23 / 29	<0.001
Triglycerides (mmol/L)	1.5 (1.1–2.0)	1.1 (0.9–1.5)	<0.001
HDL (mmol/L)	1.2 (1.1–1.3)	1.4 (1.1–1.5)	0.047
2h post-OGTT glucose (mmol/L)	6.6 ± 1.7	6.1 ± 1.3	0.053

Table 4 summarizes the multivariate analysis. The presence of AN (OR 2.4, 95% CI 1.45–3.95; P<0.001), older age (OR 1.18, 95% CI 1.06–1.29; P=0.002), higher BMI z-score (OR 7.1, 95% CI 3.3–14.5; P<0.001), and higher triglyceride levels (OR 1.88, 95% CI 1.30–2.70; P<0.001) were significant independent predictors of IR. HDL cholesterol and 2-hour post-OGTT glucose showed borderline associations. The Hosmer-Lemeshow test indicated good model fit (P=0.32).

Discussion

Obesity is one of the main public health issues that has been of great concern globally, reaching epidemic proportions. In primary care settings, identifying acanthosis nigricans (AN) in overweight and obese children provides an opportunity for early intervention aimed at preventing diabetes mellitus (DM) and other related cardiometabolic comorbidities [10-18]. The inspection for AN, specifically, over the neck, is easy and it seems non-invasive and well accepted by children. Moreover, the presence of AN serves as a useful clinical indicator to start counselling on lifestyle changes [5,19,20]

In our study, the observed prevalence of AN was 55%, which aligns with data reported in similar pediatric populations [21,22]. This highlights the high frequency of AN in children with obesity and overweight in Iraq, this state its value as a clinical marker of underlying metabolic problems [23,24].

In this study, the presence of AN showed no sex distinction which is similar findings to other huge pediatric cohorts. Both this study and other similar studies showed high possibility that obese subjects presented with AN more than overweight ones. [5,10,11].

While insulin resistance (IR) is a important mark in obesity, it is also linked with other metabolic irregularities as well as clinical and subclinical heart diseases. The usage of HOMA-IR provide measures of IR in children and serve as a physiological value of glucose homeostasis(23,24).

There is no global consensus on the precise cut-off for IR in children; some studies use values as low as 2.7, while others suggest that an HOMA-IR value of 4 may be appropriate during puberty due to transient physiological insulin resistance[12,13]. Although our study did not assess pubertal stage, we adopted a conservative threshold of HOMA-IR ≥4, consistent with large pediatric trials.

In our cohort, 29% of children met this IR criterion, with a significantly higher mean HOMA-IR value observed in those with AN compared to those without. IR was more prevalent in adolescents in comparison to younger children (37% to 25%) and in obese children compared to overweight ones (35% vs. 19%). These findings align with previous research suggesting that prolonged obesity and pubertal physiological changes contribute to increased insulin resistance and AN. The presence of IR in 25% of the younger children of (5–11 years old) overweight/obese children indicates that metabolic derangements may begin early in childhood, highlighting the need for early screening.

The study also established that IR and other cardiometabolic comorbidities were highly present among subjects with AN. The connection of AN with hypertension was less visible in comparison to its association with fatty liver disease and abnormal glucose homeostasis, but evidence of connection between blood pressure and insulin levels remains unclear. Some studies indicate a shared genetics to both IR and the hypertension; while other studies suggest additional mechanisms(25-29).

Dyslipidemia is a factor that plays a crucial role towards the development of cardiovascular diseases. High triglycerides and low high-density lipoprotein (HDL) cholesterol levels are main components of metabolic syndrome which occur in both adults and children(7,16). Both triglyceride and HOMA-IR have been recognized as important predictors of elevated carotid intima-media thickness, which regarded as a non-invasive way to diagnose the subclinical atherosclerosis in children(3). Fatty liver disease, which include, non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), is resulted from fat accumulation within the liver with or without liver cell being damaged(18). Children with AN in our study exhibited higher alanine aminotransferase (ALT) levels and a greater proportion had fatty liver on ultrasound. However, prior research has questioned the reliability of AN as an IR marker in biopsy-proven NASH cases, suggesting that liver enzyme elevation alone may be insufficient for NAFLD diagnosis. Ultrasound screening was performed only in children with elevated ALT in

our study, and although various prediction scores for fatty liver exist, their accuracy in obese children remains limited.

The prevalence and progression of diabetes mellitus vary across ethnic groups. In our cohort, 10% of children exhibited abnormal glucose homeostasis (including impaired glucose tolerance and diabetes), which is lower than reported in some other ethnic groups such as Hispanic and African American populations. Studies from the UK have reported higher type 2 diabetes prevalence among African-Caribbean children[14,25, 26].

Higher frequencies of type 2 diabetes mellitus have been reported among African-Caribbean and South Asian populations, whereas Iraqi children, similar to other Middle Eastern and some Caucasian groups, may demonstrate intermediate frequencies[15-17]. The reasons for these inter-ethnic differences remain unclear and are unlikely to be solely genetic. Social and environmental factors, including lifestyle changes and socioeconomic status, likely play significant roles in the disease's development and progression [23]. The findings of this study also reports the increased incidence of type 2 diabetes within the children and adolescents in the country. This should serve as a warning bell among the healthcare workers and professionals to focus on early detection of acanthosis nigricans as sign of abnormal glucose metabolism .

The role of insulin resistance in cardiometabolic irregularities has caused great concern and it is receiving much attention in recent years [27]. Conversely, there is no prediction model for insulin resistance existing at present for Iraqi children and adolescents. The integration of clinical, anthropometric, and biochemical markers may create a simple prediction model that can be accepted, and valuable for early identification and management of at-risk pediatric populations.

Limitations

Some of the major limitations of this study may include its retrospective design and the fact that the study was conducted at a one medical center. This limits the generalizability and prevents calculation of population-based prevalence rates. Additionally, the stage of puberty, which can significantly affect insulin resistance, was not documented. Important risk factors such as family history, maternal gestational diabetes, metabolic disorders, socioeconomic status and duration of diabetes were not part of the analysis. As it was observed in other studies and the complete information of all children cannot be obtained. Specifically, acanthosis nigricans status was missing for 2% of patients, and HOMA-IR data were absent in approximately 8%, potentially introducing selection bias.

The clinic-based sample may also overestimate morbidity compared to the general Iraqi pediatric population [24,29]. The growth references and BMI cut-offs used were based on older international or regional standards; however, these may not perfectly reflect the current Iraqi pediatric population. The lack of locally validated growth charts and consensus on overweight and obesity thresholds poses challenges for direct comparisons with other studies and may affect the interpretation of prevalence and risk factors in Iraqi children.

Conclusion

Obese children in Iraq with acanthosis nigricans (AN) face significant risk of developing insulin resistance and other cardiometabolic comorbidities. Primary care professionals and pediatricians should aware of this important clinical sign in overweight and obese children and adolescents. The presence of AN should be identified earlier in order to take appropriate intervention measures to prevent type 2 diabetes and other metabolic disorders, however, longitudinal studies need to be encouraged to create a better understanding of relationship between AN and cardiovascular and metabolic diseases.

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