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Research paper

Evaluation of depressive symptoms in obese patients with or without acanthosis nigricans

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ABSTRACT

OBJECTIVE: Acanthosis nigricans (AN) has been closely associated with obesity. Depression has also been shown to be disproportionally prevalent among obese people. However, there is still a paucity of studies on the relationship between depressive symptoms and AN in obese patients. This study examined the difference in metabolic disorders and depressive symptoms between simple obesity and obesity-related AN. METHODS: A total of 88 obese patients treated in our department were selected for analysis. They were divided into simple obesity (OB n=30) and obesity with acanthosis nigricans (AN n=58). A control (CON) group included 56 normal weight healthy volunteers. The self-administrated Beck Depression Inventory-II questionnaire was used. General characteristics and clinical data were collected for analysis. RESULTS: The frequency of depressive symptoms was recorded as 67.2% in the AN group, 43.4% in the OB group, and 3.6% in the CON group (P <0.001). The severity of depression in the AN group was significantly higher than in the OB group and CON group (P <0.001). Patients with moderate depressive symptoms had higher levels of inflammatory markers than those with mild symptoms depression. Free fatty acid (FFA) and uric acid (UA) level in the AN group were significantly increased compared with the OB group (P=0.010, P=0.020). Discrimination was associated with depressive symptoms (P <0.001). CONCLUSION: Obese patients had a higher risk of depressive symptoms, which were even higher in patients with AN. AN is associated with more depressive symptoms and high inflammation status. Psychological intervention should be started early to prevent further physical and pathological impairment in obese patients, especially obese patients with AN.

Key words: Acanthosis Nigricans, Depressive symptoms, Obesity

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INTRODUCTION

It was estimated that obesity was responsible for approximately 365,000 preventable deaths in United States in 2000.[1,2] Between 1980 and 2004, the prevalence of obesity doubled from 15% to 33% in adults and the prevalence of overweight tripled from 5.5% to 17% in children.[3] Projections based on the National Health and Nutrition Examination Surveys (NHANES) predict that if the current trends continue, more than half (51.1%) of US adults are likely to be obese and 86.3% are likely to be overweight or obese by 2030.[4]

It was postulated that obese people suffer mentally and emotionally from their weight condition because of negative perception.[5] Studies have shown that obese individuals are the last acceptable targets of discrimination.[6,7]

Acanthosis nigricans (AN) is common in obese patients and is characterized by hyperpigmented, usually brownish black papillomatous velvety thickening of the epidermis that primarily affects the axillae, posterior neck fold, flexor skin surfaces, umbilicus, and occasionally mucosal surfaces.[8,9] The cause of AN has been reported to be hyperinsulinemia, which arises as a consequence of insulin resistance associated with obesity.[8] Meanwhile, other studies have demonstrated an association of AN with hyperinsulinemia and type two diabetes mellitus (T2DM), and the recent increase of T2DM among children and youth has heightened interest in children's health, including screening children for AN as a risk factor for diabetes.[8,9] Based on related studies, it is not surprising that AN has been strongly associated with metabolic abnormalities.[10,11] But studies focusing on the relation between AN and depressive symptoms in obese patients are still lacking.

We sought to examine how AN affects the metabolism and depressive symptoms of obese patients. This research is based on a subsample of a perspective, randomized study. We hypothesize that obese patients with AN have a higher risk of metabolic abnormalities and depressive symptoms.

PARTICIPANTS AND METHODS

Participants

A total of 88 patients with obesity who had been treated in our department (Department of Endocrinology and Metabolism, Shanghai Tenth People's Hospital, Tongji University School of Medicine, Shanghai, China) were selected for participation in this study as well as 56 healthy volunteers aged from 17 to 32 years old. The participants were divided into three groups: obesity group (n = 30, BMI >28kg/m^2, no acanthosis nigricans, OB), obesity with acanthosis nigricans group (n = 58, BMI >28kg/m^2, with acanthosis nigricans, AN), and normal control (CON) group (BMI <25kg/m^2, n = 56, aged >18 years, CON). The study was approved by the Ethics Committee and the Clinical Registration Number is ChiCTR-OCS-12002381. Informed consent was obtained from each of the participants.

Inclusion criteria: Obesity was assessed according to the guidelines for prevention and control of overweight and obesity in Chinese adults.[12] The following scale for AN was used.[13] Neck severity: 0, Absent or not detectable on close inspection1; 1, Present: clearly present on close visual inspection, not visible to the casual observer, extent not measurable; 2, Mild: limited to the base of the skull, does not extend to the lateral margins of the neck (usually <3 inches in breadth); 3, Moderate: extending to the lateral margins of the neck (posterior border of the sternocleidomastoid, usually 3-6 inches), should not be visible when the participant is viewed from the front; 4, Severe: extending anteriorly (>6 inches), visible when the participant is viewed from the front**.** Axilla severity: 0, Absent: not detectable on close inspection; 1, Present: clearly present on close visual inspection, not visible to the casual observer, extent not measurable; 2, Mild: localized to the central portion of the axilla, may have gone unnoticed by the participant; 3, Moderate: involving entire axillary fossa, but not visible when the arm is against the participant's side; 4, Severe: visible from front or back in the unclothed participant when the arm is against the participant's side. In this study, each subject enrolled with AN had a score greater than 2. All subjects had completed secondary or higher education.

METHODS

Height, weight, and waist circumference were directly measured by trained technicians and body mass

index (BMI) was calculated as weight in kilograms divided by height in meters squared. Body fat percentage, visceral fat fraction, basal metabolic rate, and body age were measured with light clothes and without shoes by Omron HBF-358 (Q40102010L01322F, Japan). For all participants, morning fasting venous blood, serum specimens, total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL), high density lipoprotein cholesterol (HDL), free fatty acids, and uric acid were collected, and the blood glucose and insulin at 0min, 30min, 60min, 120min, and 180min were also measured after a 75g oral glucose tolerance test (OGTT).

The homeostasis model of assessment for insulin resistance (HOMA-IR) was calculated on the basis of fasting values of plasma glucose and insulin according to the HOMA model formula: HOMA-IR = fasting insulin * fasting glucose, divided by 22.5.[14] Significant insulin resistance was considered to be present when HOMA-IR was >1.64.[15]

Assessment of depressive symptoms

The Beck Depression Inventory-II (BDI-II) was used in this study.[16] The Chinese version of BDI-II is translated from the original version and has been widely used in China.[17] The BDI-II measures symptoms of depression based on 21 items corresponding to physical function, mood, and cognitive functioning, each question offering four possible responses which are scored from zero to three. For each individual item, a score of 0 denotes "I am not depressed", while a score of 3 denotes "I am extremely depressed". Higher scores represent greater depressive symptoms. 0-13: indicates minimal depressive symptoms, 14-19: indicates mild depressive symptoms, 20-28: indicates moderate depressive symptoms, 29-63: indicates severe depressive symptoms.

Forty-seven (47) of the 54 participants with depressive symptoms were further analyzed for risk factors of depressive symptoms; the other 7 were not included because of the patients' refusal. Risk factors of depressive symptoms for analysis included sex, education, job, monthly average household income, quality of sleep, experience of discrimination and other negative life events. The Pittsburgh sleep quality index (PSQI)[18] was used to measure the quality of sleep. The discrimination scale described by Williams and Smith was used.[19,20] Frequency ranging from "almost everyday" to "a few times a year" was defined as meaning "Yes", and "less than one a year" and "never" meant "No".

STATISTICAL ANALYSIS

Comparative analysis to identify differences was performed with the χ^2 test or Fisher's exact test on categorical variables and Student's t test or the Mann-Whitney U test on continuous variables. The one-way ANOVA test was used to measure the difference among three groups. All statistical tests were two-sided, and a two-tailed p value of less than 0.05 was considered statistically significant. All statistical analysis was performed with SPSS version 16.0 for Windows (SPSS Inc, Chicago, IL).

RESULTS

There were overall 54 individuals with at least mild depressive symptoms, 52 obese patients, and 2 volunteers. Among the 54 participants, 47 participants completed the analysis of risk factors for depressive symptoms and the result demonstrated that experience of discrimination due to obesity was associated with mild or greater depression symptoms in this cohort (Table 1). There was no significant difference in the experience of discrimination between the AN and OB groups (P =0.365).

Table 2 depicts the BDI-II score and depressive symptoms among different groups. The occurrence of depressive symptoms among the three groups was significantly different. Obese patients had higher BDI-II scores and a higher rate of depressive symptoms. AN patients had a higher BDI-II score and a higher rate of depression symptoms than the OB group (P<0.001). There were no severe depression symptoms in this series. In AN, the rate of depressive symptoms was 67.2%, significantly higher than that in OB, P=0.040, and the mean scores of the three groups were 14.4±4.9, 11.8±5.9 and 6.6±3.1, respectively (Table 2).

Compared with the CON group, the neck circumference, waist circumference, hip circumference, waist-to-hip ratio, percentage of body fat, visceral fat fraction, basal metabolic rate, body age, and BMI were increased in the AN and OB groups (OB vs CON

Table 1. Risk factors of depressive symptoms

	No.	%	P value
Sex			0.183
Male	11	24.4	
Female	36	36.4	
Education			0.792
<high school	17	33.3	
high school	17	35.4	
>high school	13	28.9	
Stable job			0.285
Yes	23	37.7	
No	24	28.9	
Monthly average household income			0.555
Low	18	28.1	
Medium	17	37.8	
High	12	34.3	
Quality of sleep			0.722
Poor	21	34.4	
Good	26	31.3	
Experience of discrimination because of obesity			0.000
Yes	36	48.6	
No	11	15.7	
Experience of other negative life events			0.793
Yes	7	36.8	
No	40	32.0	

P<0.001, AN vs CON P<0.001), though there were no significant differences between the two groups. Blood test results showed OB and AN patients had increased serum levels of C-reactive protein (CRP) (OB vs CON P=0.001, AN vs CON P<0.001), total cholesterol (TC) (OB vs CON P=0.002, AN vs CON P<0.001), triglyceride (TG), uric acid (UA), HOMA-IR (OB vs CON P<0.001, AN vs CON P<0.001), and blood glucose at each time point compared with CON group (OB vs CON P<0.001, AN vs CON P<0.001 at 0, 60, 120min, P=0.021 at 30min and 0.016 at 180min). The OB group had decreased serum levels of thyroid stimulating hormone (TSH) (P=0.004) and increased plasma insulin concentrations at 0min and 180min (P<0.001) than the CON group. In addition, the AN group had higher levels of FFA (P=0.010), UA (P=0.020), and plasma insulin concentrations at 30min and 60min than OB (P=0.011, P=0.023) at each point than CON group (P<0.001) (Table 3).

We also compared the biochemical parameters in patients with mild depressive symptoms (n=43) and with moderate depressive symptoms (n=11): the two groups had significant differences in BMI (P=0.02), FFA (P=0.010), and UA (P=0.02), while CRP, TC, TG, FPG, TSH showed no significant difference (Table 4). Table 5 depicts the correlations between BMI, depression severity, insulin resistance (HOMA-IR), CRP, and severity of AN group. The results showed that AN group was associated with depression, BMI, and HOMA-IR (correlation index was 0.367, 0.508, and 0.445, respectively) (P<0.001). In addition, depression was associated with BMI and HOMA-IR (correlation index was 0.345 and 0.306, respectively) (P<0.001). BMI was associated with HOMA-IR and CRP (correlation index was 0.670 and 0.440, respectively) (P<0.001). HOMA-IR was associated with CRP (correlation index was 0.406) (P<0.001).

Monthly average household income low: 800-1200

Table 2. Comparison of BDI-II scores and depressive symptomatology rates between the three groups

	AN N=58	OB N=30	CON N=56	P value
Score	14.4±4.9	11.8±5.9	6.6±3.1	0.000
Minimal depression	19 (32.8%)	17 (56.7%)	54 (96.4%)	<0.001
Depression	39 (67.2%)	13 (43.3%)	2 (3.6%)	<0.001
Mild depression	30 (51.7%)	11 (36.7%)	2 (3.6%)	
Moderate depression	9 (15.5%)	2 (6.7%)	0	
Severe depression	0	0	0	

OB: obese without acanthosis nigricans; AN: obese group with acanthosis nigricans; CON: control. One-way ANOVA was used to identify the difference.

Table 3. Comparison of patients' characteristics and blood test results

	OB N=30	AN N=58	CON N=56
M/F	0.5	0.7	0.5
Age (year)	25.9±8.3	26.6±9.5	24.4±7.6
Height (cm)	164.7±6.4	166.4±8.2	162.1±5.3
Neck circumference (cm)	38.8±3.5[b]	38.3±5.3[b]	31.1±2.6
Waist circumference (cm)	101.2±6.6[b]	104.7±16.4[b]	71.2±6.0
Hip circumference (cm)	105.0±5.9[b]	111.1±16.4[b]	92.1±3.0
Waist/Hip ratio	0.94±0.07[b]	0.97±0.06[b]	0.77±0.05
Percentage of body fat (%)	36.4±4.5[b]	36.2±4.2[b]	25.1±4.5
Visceral fat fraction	16.2±5.4[b]	15.8±6.9[b]	3.6±3.6
Basal metabolic rate (kcal)	1725.6±188.5[b]	1769.4±323.3[b]	1249.0±160.2
Body age (year)	59.1±10.0[b]	55.0±11.9[b]	25.0±5.1
BMI	32.86±4.14[b]	34.92±6.57[b]	21.14±1.97
FFA (mmol/l)	0.58±0.18	0.71±0.21[a,c]	0.540±0.21
CRP (mg/l)	4.33±2.97[b]	10.71±30.4[b]	0.394±0.35
UA (umol/l)	377.59±71.19[b]	445.00±112.3[b,c]	268±67.70
TC (mmol/l)	5.19±1.87[b]	5.02±1.13[b]	4.19±0.80
TG (mmol/l)	2.34±1.69[b]	1.94±1.28[b]	0.90±0.80
TSH (mIU/l)	1.96±1.19[b]	2.68±1.25	3.08±1.62
Blood glucose (mmol/l)			
(OGTT:0 min)	5.95±1.71[b]	5.82±1.56[b]	4.70±0.22
(OGTT:30min)	10.18±3.76[b]	9.41±2.36[a]	7.69±1.02
(OGTT:60min)	11.74±4.74[b]	10.20±3.75[b]	6.14±1.37
(OGTT:120min)	10.06±6.07[b]	8.62±4.23[b]	4.81±0.81
(OGTT:180min)	7.18±5.26[b]	6.46±3.89[a]	3.83±0.83
Plasma insulin (mU/l)			
(OGTT:0 min)	23.84±11.84[b]	30.88±15.12[b]	9.68±3.33
(OGTT:30min)	78.52±47.43	191.35±128.16[b,c]	107.29±46.16
(OGTT:60min)	113.56±68.52	206.39±121.43[b,c]	84.92±61.67
(OGTT:120min)	131.50±103.06	160.16±145.39[b]	57.93±35.21
(OGTT:180min)	65.01±46.05[b]	71.57±56.60[b]	17.68±21.99
HOMA-IR	6.23±3.28[b]	8.24±5.43[b]	2.03±0.74

OB: obese without acanthosis nigricans; AN: obese group with acanthosis nigricans; CON: control; BMI: Body Mass Index; M/F: Male/Female; FFA: Free fatty acid; CRP: C reactive protein; UA: Uric Acid; TC: total cholesterol; TG: triglyceride; FPG: fast plasma glucose; TSH: Thyroid stimulating hormone; HOMA-IR: homeostasis model of assessment for insulin resistance. vs CON, [a]P<0.05, [b]P<0.01; vs OB, [c]P<0.05, [d]P<0.01. Student's t test or Mann-Whitney U test were used to identify the difference.

yuan, medium: 1200-2000 yuan, high: >2000 yuan; the Pittsburgh sleep quality index (PSQI)[18] was used to measure the quality of sleep: a score >8 indicates poor quality sleep, a score <8 indicates good quality sleep. Discrimination, a measure of major experience of unfair treatment, included 9 items and their frequency;[19,20] the frequency ranged from almost every day to a few times a year, signifying Yes, otherwise less than one

Table 4. Comparison of biochemical parameters in participants with different degrees of depressive symptoms

	Mild N=43	Moderate N=11	P value
BMI	33.6±3.1	38.2±6.8	0.020
FFA	0.6±0.2	0.8±0.2	0.010
CRP	4.5±2.4	17.0 ±44.5	0.655
UA	410.7±81.6	491.7±123.5	0.020
TC	5.0±1.4	4.9±1.2	0.993
TG	1.9±1.5	1.7±0.7	0.948
FPG	6.2±2.2	6.9±4.0	0.914
TSH	2.6±1.1	2.5±1.5	0.990

Compared with patients with mild depressive symptoms (n=43), the patients with moderate depressive symptoms (n=11) had a higher level of BMI, FFA, and UA. Mann-Whitney U test was used to identify the difference.

a year and never, signifying No. Experience of other negative life events was defined as experience of at least one negative life event, including divorce, the death of parents or spouse. The χ^2 test was used to analyze the difference.

DISCUSSION

In recent years, China's rapid economic development has led to a sharp increase in caloric intake and in the proportion of individuals living a sedentary lifestyle. Obesity has therefore become a challenging health problem for adults as well as children. Obese patients suffer from discrimination and prejudice in all aspects of life from obviously unfair treatment in employment, education, etc.[21] Discrimination is harmful to its victims in many ways and can have enduring effects.[22] It has been reported that the social prejudice and discrimination experienced by obese individuals leads to chronic tension and anxiety, resulting in many negative effects.[23] Other studies have reported that exposure to weight-related teasing and anti-fat attitudes among adolescents typically results in depression and decreased self-esteem. Obese preschoolers have higher levels of emotional distress and psychiatric problems, and obese adults have a higher incidence of depression.[24-29] Our study confirmed that depressive symptoms were associated with the experience of discrimination.

The general incidence of depression is under 5%. The rates of depression among obese individuals are about 1.5 to 2 times those of individuals of normal weight.[30-32] Our study showed a high proportion of depressive symptoms in obese patients, which increased with the appearance of AN. The obese patients in the present study required treatment from a medical professional and therefore may suffer more than those who did not seek medical care.

Interestingly, in our study the discrimination experienced by individuals in the AN group and OB group did not exhibit a significant difference, which indicated that there were other factors that may bring about depressive symptoms. Studies have shown that higher levels of pro-inflammatory cytokines are found in depressed patients[33] and that those cytokines can induce somatic symptoms common in depression, such as fatigue and appetite disturbances, which in turn contribute to obesity.[34] In our study significant differences were observed in the levels of FFA, UA, and plasma insulin concentrations between AN and OB. Moreover, when we compared biochemical parameters between mild depression and moderate depression, there was a significant difference in terms of BMI, FFA, and UA ($P < 0.05$). These results indicate that a higher risk of depressive symptoms in AN may be associated with worse metabolic dysfunction. In addi-

Table 5. Correlation of different variables (n=144)

	AN symptoms	Depression	BMI	HOMA-IR	CRP
AN symptoms	1	0.367*	0.508*	0.445*	0.080
Depression	0.367*	1	0.345*	0.306*	-0.011
BMI	0.508*	0.345*	1	0.670*	0.440*
HOMA-IR	0.445*	0.306*	0.670*	1	0.406*
CRP	0.080	-0.011	0.440*	0.406*	1

*P <0.01, correlation is significant at the 0.01 level (2-tailed). AN symptoms measured by a score mentioned previously; score ranged from 2 to 4.

tion, AN symptoms were closely associated with BMI. However, whether there is causality between depressive symptoms and metabolic disorders or whether the effect is bidirectional still needs to be investigated.

Epidemiological studies have demonstrated that the incidence of AN in the general population is 7%, while it is present in up to 74% of obese people, with obesity being recognized as the most common etiological factor.[35] Furthermore, studies have demonstrated that AN is linked to insulin resistance.[36,37] In obesity, AN is a physical marker of insulin resistance and of more profound metabolic alterations. Indeed, AN is frequently associated with the metabolic syndrome.[38,39] The importance of our finding is that physicians should be aware of the existence of depressive symptoms which may be more severe if AN is also present and may exist in combination with more severe metabolic dysfunction and difficulty in losing weight. Psychological intervention should be recommended as one of the treatment methods to support and improve the lives of these patients.

There are several limitations in this study. First of all, the number of patients in this study is relatively small and larger studies are needed to confirm these results. Secondly, a selection bias may exist as this population represented only those obese patients who had the motivation to seek medical care.

In conclusion, the risk of having depressive symptoms is high in obese patients who require intervention. Discrimination is associated with depressive symptoms in obese patients. Compared with OB, AN is associated with more severe metabolic disorders and more depressive symptoms. Surveillance of depressive symptoms is recommended in obese patients, while psychological intervention is also recommended in this group of patients.

COMPETING INTERESTS

The authors declare that they have no conflict of interest.

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