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Original Article

Obese/overweight and the risk of acne vulgaris in Chinese adolescents and young adults

華裔青少年和青壯年中的肥胖/超重與尋常痤瘡的風險

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Background: An association between obese/overweight and acne vulgaris has long been postulated, but with controversial results. ***Aim:*** This study was designed to investigate the relationship between acne vulgaris, body mass index (BMI), and family history of related metabolic disorders in Chinese. ***Methods:*** We conducted a case-control study of risk factors for acne in a Chinese Han population aged 10 to 25 years attending outpatient departments in PR China. A total of consecutive 364 patients with acne were recruited, while 295 non-acne patients or healthy subjects served as controls. ***Results:*** The mean BMI was higher in moderate to severe acne patients (Pillsbury grading scale, grades 3 and 4) (21.86±2.83 kg/m^2) than controls (20.22±2.43 kg/m^2) (P<0.001). Moderate to severe acne was positively associated with overweight and obesity in people aged 18-25 years, with a more pronounced effect in women [Odds ratio (OR) 14.526, 95% confidence interval (CI) 2.961-71.272, P<0.001] than in men (OR 3.528, 95% CI 1.553-8.014, P=0.002). Body mass index in patients with thorax-back lesions were higher (22.30±2.57 kg/m^2) than patients without thorax-back lesions (20.68±2.23 kg/m^2) (P<0.001) and the relationship between thorax-back acne and overweight was observed (OR 4.480, 95% CI 2.182-9.196, P<0.001). Presence of family history of metabolic disorders such as hypertension (OR 3.511, 95% CI 1.977-6.233, P<0.001), diabetes (OR 2.697, 95% CI 1.565-4.647, P<0.001), overweight and obesity (OR1.844, 95% CI 1.242-4.407, P=0.032) were also found to be associated with increased acne severity. ***Conclusions:*** Obese/overweight in women aged 18-25 years with severe acne and family history of metabolic disorders could be risk factors of acne in Chinese acne patients.

背景：肥胖/超重和尋常痤瘡的關聯早已被假定，可是結果仍存有爭議。**目的：**本研究旨在調查華裔中的尋常痤瘡與身體質量指數及相關代謝疾病家族史的關係。**方法：**我們在中國的一個門診部門對 10-25 歲的華裔漢族進行了痤瘡危險因素的病例對照研究。總共招募了 364 名痤瘡患者，另 295 名非痤瘡患者或健康人仕作爲對照。**結果：**中度至重度痤瘡患者（皮爾斯博瑞分級量表，3級和 4 級）（21.86±2.83 公斤 / 平方米）的平均身體質量指數高於對照組（20.22±2.43 公斤 / 平方

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米）（P<0.001）。中度至重度痤瘡在 18-25 歲人群組與超重和肥胖呈正相關，當中的女性更爲顯著〔比值比（OR）14.526 ， 95% 置信區間（CI）2.961-71.272 ， P<0.001〕，大幅拋離男性（OR 3.528 ， 95% CI 1.553-8.014 ， P=0.002）。胸部背部發病者的身體質量指數（22.30±2.57 公斤 / 平方米）高於沒有胸部背部發病的（20.68±2.23 公斤 / 平方米）（P<0.001），當中亦不難察覺胸部背部痤瘡與超重之間的關係（OR 4.480 ， 95% CI 2.182-9.196, P<0.001）。代謝疾病的家族史如高血壓（OR 3.511 ， 95% CI 1.977-6.233 ， P<0.001）、糖尿病（OR 2.697 ， 95% CI 1.565-4.647 ， P<0.001），超重和肥胖（OR1.844 ， 95% CI 1.242-4.407 ， P=0.032）等都與較重的痤瘡嚴重性相關。**結論：**代謝疾病家族史及18-25歲嚴重痤瘡女患者的肥胖/超重可能是華裔痤瘡患者的危險因素。

Keywords: Acne vulgaris, BMI (body mass index), Chinese adolescent and young adults, family history of metabolic disorders, risk factors

關鍵詞：尋常痤瘡、身體質量指數、華裔青少年和青壯年、代謝疾病家族史、風險因素

Introduction

Acne vulgaris is one of the most common skin disorders affecting up to 94% of the adolescent population and frequently continues into adulthood.[1] The pathogenesis of acne is complex and multifactorial, in which excessive sebum production and its composition plays a major role.[2] Obesity is frequently accompanied by peripheral hyperandrogenism and insulin resistance, which may correlate with increased sebum production and development of severe acne.[3-5] Body mass index (BMI) is a statistical measure commonly used in measurement of overweight and obesity.[3] An association between BMI and acne has long been postulated and relevant research has been springing up during the past few years, but with controversial results.[5-9] Until now there are still no published data regarding the association between acne vulgaris and BMI in the Han population of the mainland China. The current study aimed to analyse the correlation between acne and BMI, family history of metabolic disorders, such as hypertension and diabetes in Chinese adolescents and young adults.

Materials and methods

A hospital-based case-control study of acne risk factors in a Chinese Han population aged from 10 to 25 years old attending outpatient departments in three hospitals located in two cities of PR China (Shanghai and Ningbo) from September 2014 to January 2015 was conducted. The protocol was reviewed and approved by the Human Ethics Committee of respective participating hospital. A written informed consent was obtained from the participants or their parents.

The first diagnosis of acne vulgaris was made by two board-certified dermatologists, with a final total number of 364 subjects fulfilling the inclusion/exclusion criteria. Inclusion criteria for acne cases are as follows: Chinese Han origin; age between 10 and 25 years; grade I-IV acne vulgaris as defined by Pillsbury grading scale. Exclusion criteria for acne cases: receiving systemic retinoid in the previous 6 months, oral antibiotics, hormone treatment in the previous two weeks; pregnant or breastfeeding women or the intention of becoming pregnant; or any other conditions not suitable for evaluation as determined by the physician. Two hundred and ninety-five subjects without acne who presented for health checkup or accompanying friends of patients (except family members) were recruited from the same setting during the same period with age and gender-matched, served as controls. Inclusion criteria for controls are as follows: Chinese Han origin; age between 10 and 25 years. Exclusion criteria for

controls: presenting with acne; pregnant or breastfeeding women or the intention of becoming pregnant; or any other conditions not suitable for evaluation as determined by the physician. Clinical information was collected through a standard questionnaire conducted by trained interviewers, including socio-demographic profile (age, gender), relevant medical history such as age of onset and course of acne, affected sites, severity of acne lesions, height and weight (by anthropometric measurement), menstrual history (limited to females), family history of severe acne and other major diseases (allergic disease, hypertension, diabetes mellitus and obesity) in first and/or second-degree relatives.

After anthropometric measurement, BMI was calculated and categorised according to the Cooperative Meta-Analysis Group of the Working Group on Obesity in China with recommended cut-off criteria for overweight and obesity described by Zhou et al.[10] Subjects ≥18 years old were classified into one of the following categories: underweight (BMI <18.5), normal weight (BMI: 18.5-23.9), overweight (BMI: 24-27.9) and obese (BMI ≥28). Due to the lack of general consensus on BMI thresholds in young people <18 years old, we adopted the cut-off criteria modified for overweight and obesity in Chinese people described by Group of China Obesity Task Force.[11]

The severity of acne was assessed by Pillsbury grading scale,[12] which was performed at the first time of diagnosis by two board-certified dermatologists using uniform criteria in good agreement.

Statistical analysis

The average age and average BMI were expressed as the mean ± standard deviation. Two-sample t-test was used to compare BMI between cases and controls. Comparisons of overweight/obesity, family histories of hypertension, diabetes mellitus between acne sufferers and controls were performed using chi-squared test and odds ratios (OR) as estimates of relative risks with the corresponding 95% confidence intervals (CI). Spearman's rank correlation coefficients were used to assess the relationship between BMI risk factors and acne severity. All p values were two-tailed and the level of statistical significance was set at 0.05. Analysis was performed with IBM SPSS Statistics (IBM Corp. Released 2011, version 20.0, Armonk, NY, US).

Results

The distribution of acne patients and controls according to age, gender and BMI is described in Table 1. A total of 364 patients aged from 10 to 25 years (mean age, 20.40±3.67 years, male/female=0.69) and 295 control subjects (mean age 20.79±3.29 years, male/female=0.86) were interviewed. There was no statistical significant difference in age and gender between acne patients and controls. As compared with the control group, the OR of acne patients was 1.989 (95% CI 1.148-3.445, P=0.013) in those overweight and obese subjects. The mean BMI in acne patients (20.88 ±2.32 kg/m^2) was also higher (P<0.001) than that in control subjects (20.22±2.43 kg/m^2). In patients with moderate to severe acne (Pillsbury grading scale, grades 3 and 4), the mean BMI was much higher (21.86±2.83 kg/m^2) than those in the control group (20.22±2.43 kg/m^2) (P<0.001) (Table 2). In addition, the risk of acne was also increased in those with family history of obesity (OR 1.844, 95% CI 1.242-4.407, P=0.032), diabetes mellitus (OR 2.697, 95% CI 1.565-4.647, P<0.001) and hypertension (OR 3.511, 95% CI 1.977-6.233, P<0.001).

When the distribution was stratified by gender, age (≥18 years versus <18 years) and severity of acne (grade 1-2 versus grade 3-4) simultaneously (Table 2), an increased risk of moderate to severe acne (Pillsbury grades 3 and 4) was observed in people aged 18-25 years with overweight and obesity, especially more pronounced in women (OR 14.526, 95% CI 2.961-71.272, P<0.001) than in men (OR 3.528, 95% CI 1.553-8.014,

Table 1. Comparison of the characteristics between acne patients and controls

Variables	Acne patients (n=364)	Controls (n=295)	OR (95% CI)	P value
Age (mean ± SD, year)	20.40±3.67	20.79±3.29	–	0.146
BMI (mean ± SD, kg/m^2)	20.89±2.33	20.22±2.43	–	<0.001**
Gender				
Male	148 (40.7%)	136 (46.1%)	1†	
Female	216 (59.3%)	159 (53.9%)	1.248 (0.916-1.702)	0.161
BMI categorisation (2 groups)				
Underweight and normal weight	318 (87.4%)	275 (93.2%)	1†	
Overweight and obese	46 (12.6%)	20 (6.8%)	1.989 (1.148-3.445)	0.013*
Family history				
Obesity				
No	323 (88.7%)	276 (93.6%)	1†	
Yes	41 (11.3%)	19 (6.4%)	1.844 (1.046-3.251)	0.032*
Diabetes mellitus				
No	307 (84.3%)	276 (93.6%)	1†	
Yes	57 (15.7%)	19 (6.4%)	2.697 (1.565-4.647)	<0.001**
Hypertension				
No	303 (83.2%)	279 (94.6%)	1†	
Yes	61 (16.8%)	16 (5.4%)	3.511 (1.977-6.233)	<0.001**

Chi-squared test for categorical variables, Student's t-test for quantitative variables.

BMI, body mass index; CI, confidence interval; OR, odds ratio; SD, standard deviation.

†Reference category; *P<0.05; **P<0.001

Table 2. Comparison of the characteristics between moderate to severe acne patients (Pillsbury grades 3 and 4) and controls as stratified by gender, age

Variables	Grade 3-4 acne patients (n=127)	Controls (n=295)	OR (95% CI)	P-value
Underweight and normal weight	93 (73.2%)	275 (93.2%)	1†	
Overweight and obese	34 (26.8%)	20 (6.8%)	5.027 (2.758-9.162)	<0.001**
BMI (mean ± SD, kg/m^2)	21.86±2.83	20.22±2.43	–	<0.001**
Males aged 18-25 years	**Grade 3-4 acne Patients (n=66)**	**Controls (n=107)**		
Underweight and normal weight	47 (71.21%)	96 (89.72%)	1†	
Overweight and obese	19 (28.79%)	11 (10.28%)	3.528 (1.553-8.014)	0.002*
Females aged 18-25 years	**Grade 3-4 acne Patients (n=46)**	**Controls (n=140)**		
Underweight and normal weight	38 (83.6%)	138 (98.6%)	1†	
Overweight and obese	8 (17.4%)	2 (1.4%)	14.526 (2.961-71.272)	<0.001**

Chi-squared test categorical variables, Student's t-test for quantitative variables.

BMI, body mass index; CI, confidence interval; OR, odds ratio; SD, standard deviation.

†Reference category; *P<0.05; **P<0.001

P=0.002). However, no statistical difference was noted in subjects younger than 18 years and those with mild to moderate acne (Pillsbury grades 1 and 2). Patients with chest and back acne were heavier (mean BMI: 22.30±2.57 kg/m^2) than patients without thorax-back lesions (20.68±2.23 kg/m^2) (P<0.001) and the relationship between thorax-back acne and overweight was observed (OR 4.480, 95% CI 2.182-9.196, P<0.001) (Table 3).

Table 4 shows the distribution of female patients and control subjects according to age at menarche and menstrual pattern. A relationship emerged between these variables were related with acne risk.

Discussion

In our study, we observed a greater prevalence of overweight /obesity in moderate to severe acne patients aged 18-25 years as compared to controls, especially in female patients. Even not taking into consideration of the factors of gender, age, severity of acne grading, there was still an association between BMI and acne, it was stronger in patients with thorax-back acne.

Controversial findings exist regarding the association between increased BMI and acne. In a study from Taiwan, obese women presented with less acne than in non-obese cases.[8] However, the average age of subjects in that study was 27.8 ±5.6 years (range 14-40 years old) which was older than our subjects and the subjects were females who may have had reproductive endocrine diseases which may have led to selection bias. On the other hand, a significant association between acne lesion counts and BMI in men aged 18 to 25 years, but not in those younger than 18 years, was documented in another randomised study,[9] which is consistent

Table 3. Comparison of the characteristics between moderate to severe acne patients (Pillsbury grades 3 and 4) and controls as stratified by affected sites

Variables	Patients with chest and back acne (n=46)	Patients without chest and back acne (n=318)	OR (95% CI)	P-value
Underweight and normal weight	31 (67.4%)	287 (90.3%)	1†	
Overweight and obese	15 (32.6%)	31 (9.7%)	4.480 (2.182-9.196)	<0.001**
BMI (mean ± SD, kg/m^2)	22.303±2.571	20.682±2.225	–	<0.001**

Chi-squared test categorical variables, Student's t-test for quantitative variables.
BMI, body mass index; CI, confidence interval; OR, odds ratio; SD, standard deviation.
†Reference category; *P<0.05; **P<0.001

Table 4. Comparison of the menstrual characteristics of female cases and controls

Female subjects	Cases (n=216)	Controls (n=159)	OR (95% CI)	P-value
Menstrual history				
Normal cycle pattern	148 (68.5%)	140 (88.1%)	1†	
Menstrual irregularity	68 (31.50%)	19 (11.90%)	3.385 (1.936-5.919)	<0.001**
Age of menarche (mean ± SD, year)	12.60±1.63	13.04±1.31	–	0.005

Chi-squared test categorical variables, Student's t-test for quantitative variables.
BMI, body mass index; CI, confidence interval; OR, odds ratio; SD, standard deviation.
†Reference category; *P<0.05; **P<0.001

with our study. However, females were not recruited in this randomised study. A study on Italian adolescents and young adults reported that the acne risk was reduced with lower BMI, especially in males.[7] Unlike these findings, our survey suggests the association was more significant in females.

From the controversial results mentioned above, we assumed that the impact of overweight/obesity on acne varies between adults and adolescents or between males and females, possibly due to additional factors, such as hormones, stress, cosmetics, smoking and diet. In our study, the correlation between acne and high BMI was more marked in females than in males. In young female adults (18-25 years), there has been an emphasis on underlying hormonal imbalance – hyperandrogenism.[13] In addition, we found the positive relationship between younger age of menarche, menstrual irregularity and acne, which emphasised the hormonal factors in the occurrence of acne. Androgens have been recognised to play an essential role in stimulating sebum production,[14] which plays a significant role in the pathogenesis of acne as we mentioned above. On the other hand, obesity affects sebaceous glands and sebum production,[4] thus we could point out an acne-obesity relationship. Acne is clearly aggravated by obesity-associated disorders, such as hyperandrogenism and hirsutism,[4] also as a sign of seborrhea-acne-hirsutism-androgenetic alopecia (SAHA) and hyperadrogenism-insulin resistance-acanthosis nigricans (HAIRAN) syndromes.[15] Variations in the clinical response to androgens suggest that development of acne may also be influenced by androgen bioavailability, androgenic precursors, and androgen receptor sensitivity.[16] Furthermore, androgens, insulin, growth hormone, and insulin-like growth factors are found to be elevated in obese patients,[4] and have been demonstrated to activate sebaceous glands,[16] and influence acne severity.[17]

The reason why no such relationship was found between acne and overweight/obesity for the subjects suffering from mild to moderate acne aged<18 years remains unknown, possibly because the transient decline in insulin sensitivity that occurs with the progression through puberty may trigger acne in the younger population. It is a transient decrease in insulin sensitivity in comparison to adults and pre-pubertal children,[18] combined with an increase in the serum levels of IGF-1 and insulin and a decrease in serum concentrations of sex hormone binding globulin and insulin-like growth factor (IGF)-binding protein-1.[5] Acne occurs about the same time with the gradual increase in serum insulin and in IGF-1 levels.[5,19] Insulin/IGF-1 receptor is expressed in epidermal keratinocytes.[16,20] The key regulator IGF-1 can stimulate 5α-reductase, thus promoting the synthesis of adrenal and gonadal, as well as the signal transduction of androgen receptor, accelerating the proliferation and lipogenesis of sebocytes.[21] IGF-1 also increases lipogenesis by activating PI3K Akt and MAPK ERK signal transduction pathways and induction of sterol response element-binding protein-1 (SREBP-1), which preferentially regulates genes of fatty acid synthesis. SREBP-1c is also regulated by insulin at the transcriptional level.[20] Therefore, it is possible that underlying changes in insulin metabolism may potentiate multiple factors involved in acne development. [21] High BMI is an essential factor of the metabolic syndrome, which is also associated with insulin resistance and other metabolic diseases.[5] In this way, we can further infer the close relationship between acne and high BMI.

The association was significant in patients with chest and back acne. As we observed, patients with thorax-back acne often had lesions on face, thus the observation can be explained by the association between acne involved area and overweight/obesity.

Studies on the Ache hunter-gatherers of Paraguay detected the lack of acne in association with markedly lower rates of obesity, diabetes mellitus, hypertension, hyperlipidemia, and cardiovascular diseases.[22,23] It has been suggested that acne belongs to the family of diseases of Western

civilization including obesity, type 2 diabetes mellitus and cancer.[22] Whether severe acne could serve as an early marker of some metabolic disorders remains to be proven.

There are some limitations of the current study. A selection bias in any hospital-based study design is possible. Secondly, the selection of dermatological control subjects may have resulted in some degree of overmatching if risk factors were shared among skin conditions. We tried to include control subjects from several different diagnostic categories, subjects consulting for health examination and orthopedic disorders. Thirdly, we relied solely on BMI as a surrogate measure of obesity which may not always be the best indicator for central obesity and metabolic risks. The measurement of fasting glucose, triglyceride, cholesterol, high and low density lipopropteins and waist-to-hip ratio might be more accurate in assessing the risk of increases BMI and acne. Fourthly, we used the Pillsbury grading system to evaluate the severity of acne, which is the first grading system based on an overall estimate of the acne lesion,[12] but this may not be the most precise system for acne assessment. On the other hand, a major strength of this study is that more than 95% participants who meet inclusion criteria have fulfilled the whole evaluation which can be used to adjust the estimates for several important confounders.

In conclusion, in Chinese Han adolescents and young adults, our findings provide an insight into the relationship between acne and increased BMI especially in women aged 18-25 years with severe acne, and the association was stronger in patients with thorax-back acne. Furthermore, there is an association with family history of hypertension, diabetes, overweight and obesity and acne severity. Further studies on the underlying mechanisms are needed.

Statement of ethics

The authors have no ethical conflicts to disclose.

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References

1. Ghodsi SZ, Orawa H, Zouboulis CC. Prevalence, severity, and severity risk factors of acne in high school pupils: a community-based study. J Invest Dermatol 2009;129:2136-41.
2. Zouboulis CC, Jourdan E, Picardo M. Acne is an inflammatory disease and alterations of sebum composition initiate acne lesions. J Eur Acad Dermatol Venereol 2014;28:527-32.
3. Al-Mutairi N. Associated cutaneous diseases in obese adult patients: a prospective study from a skin referral care center. Med Princ Pract 2011;20:248-52.
4. Yosipovitch G, DeVore A, Dawn A. Obesity and the skin: skin physiology and skin manifestations of obesity. J Am Acad Dermatol 2007;56:901-16; quiz 917-20.
5. Del Prete M, Mauriello MC, Faggiano A, Di Somma C, Monfrecola G, Fabbrocini G, et al. Insulin resistance and acne: a new risk factor for men? Endocrine 2012; 42:555-60.
6. Bourne S, Jacobs A. Observations on acne, seborrhoea, and obesity. Br Med J 1956;1:1268-70.
7. Di Landro A, Cazzaniga S, Parazzini F, Ingordo V, Cusano F, Atzori L, et al. Family history, body mass index, selected dietary factors, menstrual history, and risk of moderate to severe acne in adolescents and young adults. J Am Acad Dermatol 2012;67:1129-35.
8. Yang JH, Weng SL, Lee CY, Chou SY, Hsu CS, Hsu MI. A comparative study of cutaneous manifestations of hyperandrogenism in obese and non-obese Taiwanese women. Arch Gynecol Obstet 2010;282:327-33.
9. Smith RN, Mann NJ, Braue A, Makelainen H, Varigos GA. A low-glycemic-load diet improves symptoms in acne vulgaris patients: a randomized controlled trial. Am J Clin Nutr 2007; 86:107-15.
10. Bei-Fan Z. Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults: study on optimal cut-off points of body mass index and waist circumference in Chinese adults. Asia Pac J Clin Nutr 2002;11 Suppl 8: S685-93.
11. [Body mass index reference norm for screening overweight and obesity in Chinese children and adolescents]. Zhonghua Liu Xing Bing Xue Za Zhi 2004; 25:97-102.
12. Witkowski JA, Parish LC. The assessment of acne: an

evaluation of grading and lesion counting in the measurement of acne. Clin Dermatol 2004;22:394-7.
13. Dreno B, Layton A, Zouboulis CC, Lopez-Estebaranz JL, Zalewska-Janowska A, Bagatin E, et al. Adult female acne: a new paradigm. J Eur Acad Dermatol Venereol 2013;27:1063-70.
14. Zouboulis CC. [The sebaceous gland]. Hautarzt 2010; 61:467-8, 470-4, 476-7.
15. Orfanos CE, Adler YD, Zouboulis CC. The SAHA syndrome. Horm Res 2000;54:251-8.
16. Zouboulis CC. The human skin as a hormone target and an endocrine gland. Hormones (Athens) 2004;3: 9-26.
17. Zouboulis CC, Rabe T. [Hormonal antiandrogens in acne treatment]. J Dtsch Dermatol Ges 2010;8 Suppl 1:S60-74.
18. Moran A, Jacobs DR, Jr., Steinberger J, Hong CP, Prineas R, Luepker R, et al. Insulin resistance during puberty: results from clamp studies in 357 children. Diabetes 1999;48:2039-44.
19. Smith RN, Mann NJ, Braue A, Makelainen H, Varigos GA. The effect of a high-protein, low glycemic-load diet versus a conventional, high glycemic-load diet on biochemical parameters associated with acne vulgaris: a randomized, investigator-masked, controlled trial. J Am Acad Dermatol 2007;57:247-56.
20. Arora MK, Yadav A, Saini V. Role of hormones in acne vulgaris. Clin Biochem 2011;44:1035-40.
21. Smith R, Mann N, Makelainen H, Roper J, Braue A, Varigos G. A pilot study to determine the short-term effects of a low glycemic load diet on hormonal markers of acne: a nonrandomized, parallel, controlled feeding trial. Mol Nutr Food Res 2008;52:718-26.
22. Cordain L, Lindeberg S, Hurtado M, Hill K, Eaton SB, Brand-Miller J. Acne vulgaris: a disease of Western civilization. Arch Dermatol 2002;138:1584-90.
23. Zouboulis CC. Acne as a chronic systemic disease. Clin Dermatol 2014;32:389-96.