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INVESTIGATIVE REPORT

Study of Psychological Stress, Sebum Production and Acne Vulgaris in Adolescents

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Sebum production is thought to play a major role in acne vulgaris in adolescents. Psychological stress may exacerbate acne; however, it is not known whether the perceived association between stress and acne exacerbation is due to increased sebum production. The aims of this study were to determine: (*i*) if psychological stress in adolescents is associated with increased sebum production; and (*ii*) if stress is associated with increased acne severity independent of, or in conjunction with, increased sebum production. Ninety-four secondary school students in Singapore (mean age 14.9 years) were enrolled in this prospective cohort study. During a high stress condition (prior to mid-year examinations) and a low stress condition (during the summer holidays), the following were evaluated: (*i*) self-reported stress level using the Perceived Stress Scale; (*ii*) sebum level at baseline and at 1 h; and (*iii*) acne severity. The prevalence of self-reported acne in this study population was high (95% in males and 92% in females). Most subjects had mild to moderate acne. Sebum measurements did not differ significantly between the high stress and low stress conditions. For the study population as a whole, we observed a statistically significant positive correlation (r=0.23, p=0.029) between stress levels and severity of acne papulopustulosa. In adolescents, psychological stress does not appear to affect the quantity of sebum production. The study suggests a significant association between stress and severity of acne papulopustulosa, especially in males. Increased acne severity associated with stress may result from factors other than sebum quantity. *Key words: acne; adolescents; sebum; psychological stress.*

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Acne vulgaris is a very common disease in adolescents, affecting over 90% of males and 80% of females in all ethnic groups (1). Acne significantly affects physical and psychosocial well-being. The pathogenesis of acne vulgaris is multifactorial, with hormones, sebum production and bacterial colonization playing major roles (2–3). Psychological stress has also been identified amongst factors that exacerbate acne (4–6). In a recent survey among 215 sixth-year medical students, 67% of the students identified stress as the cause of their acne (7). Moreover, several studies have shown that psychological stress can alter the immune functions of the skin (8) and cutaneous barrier function (9).

Despite the apparent link between stress and exacerbation of acne vulgaris (4, 5), there has been little research to elucidate the mechanisms behind this relationship; specifically whether the perceived association between stress and acne exacerbation is due to increased sebum production. This study addresses two major questions: first, are increased levels of psychological stress in adolescents associated with increased sebum production? Secondly, does stress contribute to acne severity independent of, or in conjunction with, increased sebum production?

METHODS

The study was conducted among adolescent students recruited from Choa Chu Kang Secondary School in Singapore. Of the 160 students invited to participate in the study, 94 (59%) agreed (43 men and 51 women), and all participants provided parental informed consent. The study was approved by the National Skin Centre and National Health Group Polyclinics Research Ethics Committee as well as the Singapore Ministry of Education.

Mid-year school examinations were selected as a stress model for the study. Singaporean children undergo an intensive school examination process (10). Children's long-term career prospects are highly influenced by the results of such examinations. Not surprisingly, these tests are known to induce psychological stress in Singaporean children (10, 11). This study was conducted in two phases. Phase I (the high stress condition) coincided with the school mid-year examinations and lasted for 2 weeks in May. Phase II (the low stress condition) was performed between mid-July and early August, approximately 2 months after the end of examinations.

In each phase, measurements were taken in a controlled environment of 21°C after a period of acclimatization of at least 20 min. In between measurements, students were asked to remain in another room of similar temperature and surroundings. Humidity levels are consistent throughout the year in Singapore. All measurements were collected in the afternoon, between 12:30 h and 18.00 h. Students were asked to complete a self-administered questionnaire, which included information

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on health status, medical history, smoking history, acne history, previous treatments for acne, and the nature of treatment when applicable. Students were instructed not to apply any topical medications for at least one day prior to study testing and were instructed not to wash their face with any soaps or cleansers on the day of the test. The height and weight of all examinees was recorded, and body mass index calculated.

The extent of perceived psychological stress was assessed using the Perceived Stress Scale (PSS). The PSS is a state of the art psychological test for assessing stress, comprising a 14-item self-questionnaire that assesses the perception of psychological stress and measures the degree to which the respondent's external situation is self-appraised as being stressful (12). This measure is widely used in stress research as a psychological instrument for measuring the perception of stress and has demonstrated normative data and reliability. Previous studies have used the PSS to evaluate self-reported stress in adolescents (13, 14) and college students, including stress associated with school examinations (5, 15). The PSS was administered to students at two designated time points: during the examination period (Phase I) and approximately 2 months after examinations (Phase II), which coincided with the students' summer holidays.

Sebum measurements were performed using a sebumeter (Sebumeter SM810, Courage & Khazaka, Cologne, Germany), which provides a direct measure of sebum secretion. Sebum lipids are adsorbed onto a plastic opalescent film, which is pressed against the skin, thus making it transparent. The sebumeter shines a light beam on the film, and the ratio of reflected to incident light increases proportionally with the quantity of sebum sampled. The method was originally validated by Cunliffe et al. in 1980 (16), and the measurement of skin surface lipids using a sebumeter has been well established in previous studies (17, 18).

Baseline sebum measurements were conducted in each of the 2 phases at 2 sites on the face of each subject. The first site was on the forehead at a fixed point one cm above an imaginary line between the medial boundaries of both eyebrows. The second site was on the right cheek prominence over the zygomatic process. The amount of sebum on the skin surface is known to be approximately constant with time and body site for a given individual (19). Subjects' cheeks and forehead were wiped with a blotting synthetic film (Clear & Clean oil control film, Johnson & Johnson) until the blotting paper was clear from oil stains. Sebum was measured immediately after blotting with the synthetic film and empirically graded as zero value on the sebumeter. Sebum levels were then re-measured one h later to evaluate sebum production. This process was repeated in the same manner for the second phase of the study approximately 2 months later.

Clinical classification of acne severity was based on the system proposed by Plewig & Kligman (20). Study participants' acne was classified as comedonal, papulopustular, or nodulocystic and then graded according to the number of lesions present. The severity of acne was graded by a single observer who was blinded to the study outcomes and aims for both phases.

Statistical methods

Matched analysis of the differences in PSS values between the 2 phases was carried out by Wilcoxon signed-rank test. Potential correlations between stress and sebum levels were examined in two ways. First, stress was correlated with sebum levels separately for each phase. Secondly, the change in stress levels was correlated with changes in sebum levels. Spearman's rank correlation was used in view of the ordinal nature of the PSS. Correlation between sebum levels and acne severity and between stress levels and acne severity were analysed using Spearman's rank correlation. Differences in acne severity between Phases I and II were determined using the McNemar test.

RESULTS

The demographic characteristics of the study population are provided in Table I. The mean age of both male and female subjects was 14.9 years. The prevalence of self-reported acne in our study population was high (95% in males and 92% in females). However, only 23% of the study participants ever received treatment for acne, including topical medications. None of the adolescents in the study was currently being treated with isotretinoin. As there were only 5 non-Chinese males in the sample, the effect of ethnicity on sebum levels was not considered. None of the subjects were smokers. One patient had a medical history significant for stable nephrotic syndrome and was not on oral corticosteroid treatment; therefore, his results were included in our analysis.

The severity of participants' acne during each phase of the study is shown in Table II. Of note is the absence of nodulocystic acne amongst study participants. Whether acne sufferers had comedonal or papulopustular lesions, the majority had low-grade acne (grades I and II). Sebum measurements did not differ significantly between the high stress (Phase I) and low stress (Phase II) conditions. Male and female subjects' sebum levels in each phase are presented in Table III. Matched analyses of male subjects' self-reported stress levels between the two phases using the PSS showed significantly higher stress scores in Phase I just prior to examinations compared with Phase II during low stress (p=0.03). Female subjects also demonstrated higher self-reported stress scores in Phase I vs. Phase II; however, these differences did not achieve statistical significance (p=0.10).

Table I. *Demographics and medical history of study participants (n=94)*

	Male		Female	
Physical characteristics	*n*	Mean (SD)	*n*	Mean (SD)
Age (years)	43	14.9 (0.27)	51	14.9 (0.29)
BMI (kg/m^2)*	43	21.0 (4.2)	51	19.2 (2.0)
Acne and other medical history		Proportion (%)		Proportion (%)
Ever had acne (self-reported)	41	95.3	47	92.2
Ever had acne treatment	9	20.9	13	25.5
On acne treatment now	7	16.3	7	13.7
Acne treated with antibiotics	0	0.0	2	3.9
Acne treated with topicals	7	16.3	7	13.7
Ethnicity				
Chinese	38	88.4	38	74.5
Malay	2	4.7	8	15.7
Indian	3	7.0	3	5.9
Other	0	0.0	2	3.9

*For 15-year-old male students, 10th and 90th percentile BMI (body mass index) are 17.1 and 24.6, respectively. For 15-year-old female students, 10th and 90th percentile BMI are 16.9 and 25.4, respectively.
SD: standard deviation

Table II. *Acne severity by gender under high stress (Phase I) and low stress (Phase II) conditions*

	Phase I		Phase II	
	n	Proportion (%)	*n*	Proportion (%)
Males				
Acne comedonica				
Grade I	26	60.5	23	53.4
Grade II	16	37.2	12	27.9
Grade III	0	0.0	6	13.9
Grade IV	1	2.3	1	2.3
Acne papulopustulosa				
Grade I	25	58.1	31	72.1
Grade II	11	25.6	12	27.9
Grade III	7	16.3	0	0.0
Grade IV	0	0.0	0	0.0
Females				
Acne comedonica				
Grade I	24	47.1	28	54.9
Grade II	22	43.1	18	35.3
Grade III	4	7.8	4	7.8
Grade IV	1	2.0	1	2.0
Acne papulopustulosa				
Grade I	37	72.6	46	90.2
Grade II	11	21.6	5	9.8
Grade III	2	3.9	0	0.0
Grade IV	0	0.0	0	0.0

Potential correlations between stress and sebum levels were examined in two ways. First, stress was correlated with sebum levels separately for each phase. Secondly, the change in stress levels was compared with the change in sebum levels. For most sebum measurements, no significant correlation between stress and sebum levels was observed.

Acne severity was also correlated with sebum levels under the high stress (Phase I) and low stress (Phase II) conditions. For males under high stress, there was a statistically significant positive correlation between severity of papulopustular acne and baseline and 1-h sebum levels on the cheek (p=0.005, p=0.005) and forehead (p=0.004, p=0.004). For male subjects in the low stress condition, a significant correlation was demonstrated only between acne papulopustulosa severity and 1-h forehead sebum production (p=0.007). No significant correlation was observed for acne comedonica in males under either the high stress or low stress condition.

For female adolescents, there was a positive correlation between severity of acne and sebum levels under both the high stress and low stress condition. Under high stress, there was a statistically significant positive correlation between acne comedonica severity and baseline and 1-h forehead sebum levels (p=0.007, p=0.013) as well as between acne papulopustulosa severity and baseline and 1-h cheek sebum levels (p=0.003, p=0.004). For females in the low stress condition, there was a significant positive correlation between severity of acne comedonica and baseline and 1-h sebum levels for both the forehead (p=0.000, p=0.004) and cheek (p=0.000, p=0.047).

For the study population as a whole, we observed a statistically significant positive correlation (r=0.23, p=0.029) between stress levels and severity of acne papulopustulosa. When analysed individually by gender, this correlation was not observed. No correlation was noted between subject-reported stress levels, using the PSS, and severity of acne comedonica.

Table III. *Baseline sebum levels and 1-h sebum production by gender under high stress (Phase I) and low stress (Phase II) conditions**

	Phase I		Phase II	
	Mean	SD	Mean	SD
Males				
Baseline sebum level (forehead)	153	71	155	73
Baseline sebum level (cheek)	90	56	95	63
1-h sebum production (forehead)	133	54	130	66
1-h sebum production (cheek)	82	46	90	60
Females				
Baseline sebum level (forehead)	131	69	125	66
Baseline sebum level (cheek)	71	51	77	52
1-h sebum production (forehead)	103	60	105	54
1-h sebum production (cheek)	65	45	62	41

*Sebum measurements are in arbitrary units. In the range 50–200, units closely approximate to μg/cm^2.
SD: standard deviation

DISCUSSION

Despite the high prevalence of acne vulgaris in adolescents and the numerous reports linking stress with a worsening of this condition (4–6), few studies have actually addressed the pathophysiology of this apparent link. The pathogenic factors of acne vulgaris are well understood. Previous research has examined the effect of stress on the skin microenvironment, particularly skin barrier function, cytokine secretion and T-cell activity (8–9). The current study investigated one of the factors involved in acne pathogenesis – sebum production – and how it relates to stress and exacerbation of acne. Many previous articles have described the important role of sebum production in acne pathogenesis and treatment (2, 3, 21–22). The high prevalence of acne (95% in males, 92% in females) observed in our study population is similar to values reported in previous studies (1). We demonstrated a statistically significant positive correlation between increased self-reported stress and increased severity of acne papulopustulosa.

In this large study of adolescents, self-reported stress levels in males were significantly higher under the high stress condition (Phase I) than under the low stress condition (Phase II) based on the PSS. In Phase I of the study, the PSS was administered for all study subjects on the day prior to examinations; it was therefore assumed that we would be measuring participants' stress levels at their peak. In female subjects, PSS scores were also higher just prior to examinations (Phase I)

than when returning from vacation (Phase II); however, this difference did not achieve statistical significance (p=0.10).

The significantly higher stress level in male students supports the appropriateness of the stress model for male students; however, there may be gender differences in perception of stress among adolescents. In previous research, significant gender differences have been observed in the perception of academic stress among adolescent high school students (23). A possible explanation for the lack of statistically significant differences in self-reported stress among female students could be female students' attitudes towards examinations. If female students in the study were better prepared than their male counterparts, female students may have experienced less psychological stress during examinations. Although not a component of this study, this theory could have been further evaluated by reviewing students' examination results. In addition, it has been demonstrated that psycho-neuroendocrine stress responses vary significantly across the menstrual cycle (24). Thus, the timing of the menstrual cycle is a possible confounding factor in self-reported stress levels among female subjects.

Our findings demonstrated no correlation between increased stress and sebum levels. One possible explanation for our inability to detect the expected correlation between stress and sebum levels in this study is that increased acne severity may result not from increased sebum secretion and excretion but from changes in neuropeptide secretion and sebum lipid composition. Recent studies by Zouboulis et al. (6, 28) suggest that the neuropeptide corticotrophin-releasing hormone, which has a crucial importance for cutaneous responses to stress (25–27), influences the sebaceous glands to synthesize sebaceous lipids. The role of neuropeptides has also been suggested by the detection of substance P-immunoreactive nerve fibres in close proximity to sebaceous glands (29–30). Thus, stress may affect the production of inflammatory mediators and specific lipids involved in inflammation by the sebaceous glands rather than the quantity of sebum.

Analysis of the relationship between sebum levels and acne severity in male participants during the high stress condition revealed a positive correlation between nearly all sebum measurements and severity of papulopustular acne. In males, this correlation was not observed under the low stress condition, which suggests that increased stress levels result in a positive correlation between sebum levels and severity of papulopustular lesions. The complexity of the relationship between sebum production and acne pathogenesis is supported by twin studies in which identical twins with virtually identical rates of sebum excretion demonstrated significantly different degrees of acne severity (31).

This study has several limitations. First, the vast majority of study subjects had mild to moderate acne, which is most common in the adolescent population. It is possible that more severe forms of acne might demonstrate stronger correlations with psychological stress; however, the recent study by Youn et al. (32) suggests that increased sebum levels do not directly cause development of acne lesions. Secondly, study results may have been affected by the limited participation rate (59%) among Singapore secondary school students. In the vast majority of cases, non-participation was due to inability to obtain parental consent. Finally, sebum production is known to fluctuate with seasonal variation in temperature and humidity (18). Owing to its tropical climate, however, Singapore is an ideal setting to negate such variation because temperature and humidity are consistent throughout the year.

Based on this study, increased stress does not correlate with increased sebum quantity but demonstrates a positive correlation with acne severity. It is possible that other mediators associated with psychological stress play a significant role in acne pathogenesis. It would be of particular interest to examine the relationship between stress, acne and inflammatory mediators, such as neuropeptides and specific lipids involved in acne inflammation.

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Conflict of interest: None to declare.

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