Adult female acne and associated risk factors: Results of a multicenter case-control study in Italy

Anna Di Landro, MD,[a,b] Simone Cazzaniga, MS,[a,c] Francesco Cusano, MD,[d] Angela Bonci, MD,[e] Cardinali Carla, MD,[f] Maria Letizia Musumeci, MD, PhD,[g] Annalisa Patrizi, MD,[h] Vincenzo Bettoli, MD,[i] Enrico Pezzarossa, MD,[j] Marzia Caproni, MD,[k] Anna Belloni Fortina, MD,[l] Elena Campione, MD,[m] Vito Ingordo, MD,[n] Luigi Naldi, MD,[a,b] and the Group for Epidemiologic Research in Dermatology Acne Study Group[o]

Bergamo, Benevento, Reggio Emilia, Prato, Catania, Bologna, Cremona, Ferrara, Florence, Padua, Rome, and Taranto, Italy, and Bern, Switzerland

Background: The reasons for the appearance of acne in adulthood are largely unknown.

Objective: We explored the role of personal and environmental factors in adult female acne.

Methods: We conducted a multicenter case-control study in the outpatient departments of 12 Italian cities. Cases (n = 248) were consecutive women ≥25 years of age with newly diagnosed acne of any grade. Controls (n = 270) were females diagnosed with conditions other than acne.

Results: In multivariate analysis, a history of acne in parents (odds ratio [OR] = 3.02) or siblings (OR = 2.40), history of acne during adolescence (OR = 5.44), having no previous pregnancies (OR = 1.71), having hirsutism (OR = 3.50), being an office worker versus being unemployed or being a housewife (OR = 2.24), and having a high level of reported psychological stress (OR = 2.95) were all associated with acne. A low weekly intake of fruits or vegetables (OR = 2.33) and low consumption of fresh fish (OR = 2.76) were also associated with acne.

Limitations: We did not establish an onset date for acne. Some of our associations may reflect consequences of established acne.

Conclusion: Lifestyle factors may play an important role for acne development in adulthood, but their role should be further assessed in prospective studies. (J Am Acad Dermatol 2016;75:1134-41.)

Key words: adult female acne; case-control study; diet; family history; risk factors; stress.

From the Study Center of the Italian Group for Epidemiologic Research in Dermatology (GISED)[a] and the Dermatology Unit,[b] Papa Giovanni XXIII Hospital, Bergamo; Department of Dermatology,[c] Inselspital University Hospital, Bern, Switzerland; Dermatology Units at G. Rummo Hospital,[d] Benevento, S. Maria Nuova Hospital,[e] Reggio Emilia, S. Stefano Hospital,[f] Prato, Department of Specialistic, Diagnostic and Experimental Medicine,[h] S. Orsola-Malpighi Hospital, Bologna, Istituti Ospitalieri Hospital,[j] Cremona, and the Department of Systems Medicine,[m] University of Rome Tor Vergata; Dermatology Clinic,[g] University of Catania, P.O. "G. Rodolico," A.O.U. Policlinico Vittorio Emanuele, Catania; Section of Dermatology,[i] Department of Clinical and Experimental Medicine, S. Anna University Hospital, Ferrara; Rare Diseases Dermatology and Cutaneous Immunopathology,[k] UO Dermatology I ASF-University of Florence; Pediatric Dermatology Unit,[l] Department of Medicine, University of Padua; Outpatient Department of Dermatology,[n] District No. 6, Health Local Unit, Taranto; and the Group for Epidemiologic Research in Dermatology Acne Study Group.[o]

Funding sources: None.

Conflicts of interest: None declared.

Accepted for publication June 30, 2016.

Correspondence to: Luigi Naldi, MD, Centro Studi Group for Epidemiologic Research in Dermatology, Via Garibaldi 13/15, 24122 Bergamo, Italy. E-mail: luigi.naldi@gised.it.

Published online August 16, 2016.

0190-9622/$36.00

© 2016 by the American Academy of Dermatology, Inc.

http://dx.doi.org/10.1016/j.jaad.2016.06.060

INTRODUCTION

Acne is one of the most common diseases in adolescence, affecting >80% of young people.[1] The disease usually resolves after 20 years of age, although it also affects 20% to 40% of adults. A study of people 40 to 49 years of age conducted in 1979 showed a prevalence of acne of about 3% in men and 11% to 12% in women, with a significant decrease after 45 years of age.[2] Over the last decades, the average age of people with acne has increased from 20.5 to 26.5 years.[3] In a 2001 study of 3305 women 25 to 40 years of age, the prevalence of acne was 41%,[4] and in a second study of 2895 women 10 to 70 years of age acne peaked during the teenage years, but >25% of women suffered from acne after 21 years of age, with a peak of 45% in women between 21 and 30 years of age.[5]

CAPSULE SUMMARY

- Several factors have been associated with adult acne.
- Adult female acne was associated with a family history of acne, acne in adolescence, no previous pregnancies, and lifestyle factors (eg, diet, occupation, and stress).
- Lifestyle factors should be given proper attention in the management of women with adult acne.

When the disease is present after the age of 25 years in women, it is usually named adult female acne (AFA), which is comprised of 2 variants: "persistent" acne continues after adolescence, while "late onset" acne starts after 25 years of age.[3] The latter seems to occur less frequently than the former.[6] The reasons for its increase in adulthood are unknown: endogenous and exogenous factors, such as smoking and psychological stress, can combine and contribute to its clinical expression.[7-9]

To analyze the roles played by different factors, including family history, smoking habits, occupation, comorbidities, psychological stress, and dietary factors, we conducted a case-control study of adult women who were clinically diagnosed with acne at several dermatologic outpatient clinics in Italy.

METHODS

This multicenter case-control study assessed factors associated with AFA in a consecutive group of women ≥25 years of age who attended a dermatologic outpatient department in 1 of 12 Italian cities distributed across Italy. The patients were diagnosed with acne of any grade (ranging from mild to severe), as assessed by dermatologists during the visit, while the controls were women ≥25 years of age who visited a dermatologic outpatient clinic for a condition other than acne and who were not diagnosed with acne during the visit. All patients provided written informed consent before participating in the study. The protocol was reviewed and approved by the ethics committee at each participating center.

Acne severity was defined according to a global score,[10] using photographs limited to the face to help with the assessments. The following 4 categories were considered: no or minimal acne lesions, where only a few comedones are present; mild acne, where lesions include several noninflammatory comedones with <10 inflammatory lesions; moderate acne, with many comedones, papules, and pustules but no nodules; and severe acne, with inflammatory nodules in addition to papules and pustules. The "inflammatory" form was considered when the acne was dominated by inflammatory papules and pustules[3]; this form was distinct from a "retentional" form, in which the comedones and microcysts predominated, with minimal inflammatory signs.

A standardized questionnaire was administered by dermatologists during outpatient visits and was developed to collect general sociodemographic information (eg, age, sex, education, and occupation), personal habits (eg, smoking and alcohol consumption), anthropometric measurements (eg, height and weight), pregnancy, menstrual pattern and history, use of oral contraceptives, history of adolescence acne, history of acne in relatives, relevant comorbidities (eg, polycystic ovary syndrome [PCOS], hirsutism, type II diabetes, and thyroid disease), and stress level during last month, which was self-assessed according to a 5-point scale (ie, none, mild, moderate, high, and very high).

A food frequency questionnaire was used to record information on the intake of selected food items, including the usual number of portions per week in the last month before the interview. Intakes of foods that were reported at least once a month but less than once a week were coded as 0.5 portions per week. The food groups investigated included whole, skim, or partially skim milk, other dairy products (eg, cheese and yogurt), starchy foods (eg, pasta, bread, and rice), fish, beef, chocolate, cakes and sweets, vegetables, and fruit.

Characteristics of acne (eg, severity, location, and distribution) and drugs taken for the disease were also investigated.

Table I. Demographic distribution and general characteristics of the 518 subjects included in the study, both overall and according to their case-control status

	AFA						
	No (n = 270)		Yes (n = 248)		Total (N = 518)		
	n[†]	%	n[†]	%	n[†]	%	*P* value*
Age, y (mean ± SD)	36.4 ± 7.0		32.2 ± 5.2		34.4 ± 6.6		<.001
25-29	56	20.7	86	34.7	142	27.4	
30-39	115	42.6	141	56.9	256	49.4	
40+	99	36.7	21	8.5	120	23.2	
Body mass index, kg/m^2 (mean ± SD)	22.6 ± 3.9		22.4 ± 3.9		22.5 ± 3.9		.48
<20.0	68	25.8	65	26.3	133	26.0	
20.0-24.9	147	55.7	137	55.5	284	55.6	
≥25.0	49	18.6	45	18.2	94	18.4	
Smoking habits							
No/ex-smoker	206	76.3	185	74.6	391	75.5	.65
Current smoker	64	23.7	63	25.4	127	24.5	
Drinker							
No/ex-drinker	105	38.9	90	36.4	195	37.7	.57
Occasional/regular	165	61.1	157	63.6	322	62.3	
Educational attainment							
Lower secondary school	40	14.9	26	10.7	66	12.9	.34
Upper secondary school	118	44.0	116	47.7	234	45.8	
University/doctorate degree	110	41.0	101	41.6	211	41.3	
Present or last occupation							
None/housewife	68	25.5	43	17.8	111	21.9	.10
Student	16	6.0	21	8.7	37	7.3	
Unskilled worker	28	10.5	25	10.4	53	10.4	
Office worker	110	41.2	120	49.8	230	45.3	
Manager/freelance	45	16.9	32	13.3	77	15.2	
History of pregnancy							
No	102	37.8	151	60.9	253	48.8	<.001
Yes (1+)	168	62.2	97	39.1	265	51.2	
Age at menarche, y (mean ± SD)	12.6 ± 1.5		12.4 ± 1.5		12.5 ± 1.5		.03
<12	40	18.6	59	28.2	99	23.3	
12	58	27.0	52	24.9	110	25.9	
≥13	117	54.4	98	46.9	215	50.7	

AFA, Adult female acne; *SD*, standard deviation.

*Mann–Whitney *U* test and Pearson's chi-squared or Fisher's exact tests, as required, were used to assess case-control differences in continuous and categorical variables, respectively.

[†]Numbers may not add up to the total because of missing data.

Statistical analysis

For descriptive purposes, data were presented as means with standard deviations (SD) or as numbers with percentages for continuous and categorical variables, respectively. Univariate differences between the cases and controls (across different levels of variables) were assessed using the Mann–Whitney *U* test for continuous variables and the Pearson's chi-squared or Fisher's exact tests, as required, for categorical variables. For analytical purposes, continuous variables were categorized based on clinically meaningful values or tertile data distribution as cut-off thresholds. Food variables were categorized using the first tertile of distribution as the cut-off point. All variables with a *P* value < .15 in the univariate analysis were evaluated through 4-stage hierarchical multiple logistic regression, with a forward stepwise algorithm, to assess which variables were independent factors associated with AFA. In the first stage of the model, the patients' constitutional factors (ie, acne in first-degree relatives, including parents and siblings) were evaluated; in the second stage, other general variables, including occupation, pregnancy and menstrual history, and history of adolescence acne were assessed. In the next stage of the model, relevant comorbidities and stress level during the last month were considered; in the final stage, food consumption frequencies were evaluated. Variables selected at each stage were retained as fixed factors in the next step of the algorithm. Age was included as a general fixed

Table II. Medical history, both overall and according to case-control status

	AFA						
	No		Yes		Total		
	n[†]	%	n[†]	%	n[†]	%	*P* value*
History of adolescent acne							
No	193	71.5	79	31.9	272	52.5	<.001
Yes	77	28.5	169	68.1	246	47.5	
History of acne in relatives							
No	176	65.9	118	48.0	294	57.3	<.001
Yes	91	34.1	128	52.0	219	42.7	
Parents							
No	236	89.1	175	71.7	411	80.7	<.001
Yes	29	10.9	69	28.3	98	19.3	
Siblings							
No	222	83.8	174	71.3	396	77.8	.001
Yes	43	16.2	70	28.7	113	22.2	
Cousins							
No	248	93.6	230	94.3	478	93.9	.75
Yes	17	6.4	14	5.7	31	6.1	
Uncles/aunts							
No	258	97.4	236	96.7	494	97.1	.67
Yes	7	2.6	8	3.3	15	2.9	
Comorbidities							
PCOS							
No	223	83.2	179	72.8	402	78.2	.004
Yes	45	16.8	67	27.2	112	21.8	
Hirsutism							
No	257	96.3	204	82.6	461	89.7	<.001
Yes	10	3.7	43	17.4	53	10.3	
Type II diabetes							
No	267	99.6	243	98.0	510	98.8	.11
Yes	1	0.4	5	2.0	6	1.2	
Thyroid disease							
No	228	84.4	213	86.2	441	85.3	.57
Yes	42	15.6	34	13.8	76	14.7	
Other diseases							
No	209	78.9	190	78.5	399	78.7	.92
Yes	56	21.1	52	21.5	108	21.3	
Menstrual pattern[‡]							
Regular	202	78.0	189	77.5	391	77.7	.89
Irregular	57	22.0	55	22.5	112	22.3	
Use of oral contraceptives							
No	203	76.9	185	74.6	388	75.8	.54
Yes	61	23.1	63	25.4	124	24.2	
Stress during last month							
No/mild	90	34.0	51	20.9	141	27.7	.001
Moderate	117	44.2	113	46.3	230	45.2	
High/very high	58	21.9	80	32.8	138	27.1	

AFA, Adult female acne; *PCOS*, polycystic ovary syndrome.
*Pearson's chi-squared or Fisher's exact tests, as required, were used to assess case-control differences.
[†]Numbers may not add up to the total because of missing data.
[‡]Postmenopausal women were excluded.

adjustment factor in the models. The effects of the identified factors were presented as odds ratios (ORs), with 95% confidence intervals (CIs) and *P* values. Patients with missing data were excluded from the analysis. All tests were considered to be significant at $P < .05$. The analyses were performed using SPSS software (version 20.0; IBM Corporation, Armonk, NY).

Table III. Food intake frequency, both overall and according to case-control status

	AFA						
	No		Yes		Total		
	n[†]	%	n[†]	%	n[†]	%	*P* value*
Milk (days/week)							
≤3	114	42.2	116	48.1	230	45.0	.18
>3	156	57.8	125	51.9	281	55.0	
Milk type							
Skimmed	34	17.9	31	18.5	65	18.2	.96
Partially skimmed	112	58.9	100	59.5	212	59.2	
Whole	44	23.2	37	22.0	81	22.6	
Dairy products (days/week)							
≤3	126	46.7	124	51.5	250	48.9	.28
>3	144	53.3	117	48.5	261	51.1	
Starchy foods (days/week)							
≤3	41	15.2	42	17.4	83	16.2	.49
>3	229	84.8	199	82.6	428	83.8	
Cakes and sweets (days/week)							
≤3	160	59.3	150	62.2	310	60.7	.49
>3	110	40.7	91	37.8	201	39.3	
Chocolate (days/week)							
≤3	184	68.1	176	73.0	360	70.5	.23
>3	86	31.9	65	27.0	151	29.5	
Vegetables and fruit (days/week)							
≤3	31	11.5	46	19.1	77	15.1	.02
>3	239	88.5	195	80.9	434	84.9	
Fish (days/week)							
≤3	227	84.1	217	90.0	444	86.9	.05
>3	43	15.9	24	10.0	67	13.1	
Beef (days/week)							
≤3	213	78.9	193	80.1	406	79.5	.74
>3	57	21.1	48	19.9	105	20.5	

AFA, Adult female acne.
*Pearson's chi-squared or Fisher's exact tests, as required, were used to assess case-control differences.
[†]Numbers may not add up to the total because of missing data.

RESULTS

Demographics and clinical characteristics

From February 2013 to January 2015, 518 women (248 cases and 270 controls) were included in the study. Table I shows the demographic distribution and general characteristics of the subjects according to their case or control status. Overall, the mean age was 32.2 ± 5.2 and 36.4 ± 7.0 years (mean ± SD) for cases and controls, respectively ($P < .001$), and the mean body mass index (BMI) was 22.5 ± 3.9 kg/m^2. A total of 24.5% of the women were current smokers, and 62.3% were regular or occasional drinkers, with no significant differences between the cases and controls. A large proportion of the women reported attending upper secondary school or having a university degree (87.1%), and many (45.3%) worked as office workers; the differences between the cases and controls did not reach the level of significance ($P = .10$). A history of previous pregnancy was present in 39.1% of the cases compared to 62.2% of the controls ($P < .001$), and the age at menarche was slightly lower among the cases compared to the controls ($P = .03$).

Most of the cases had moderate (50.2%) or mild acne (42.0%), with only 19 patients (7.8%) showing signs of severe acne. Inflammatory acne was the most common clinical form (75.2%), and most of the subjects had facial lesions (96.8%), particularly on the cheeks (74.7%) and chin (71.3%), with an average number of 16.6 ± 11.3 lesions. In addition, 30.4% of the patients had lesions located on their trunks. The most common lesions observed were papules (35.4%), pustules (32.1%), and comedones (30.0%). The mean age of current acne onset was 30.5 ± 6.4 years. Controls were mainly visited for pigmentary lesion screening (36.3%), warts (5.6%), dermatitis/eczema (5.2%), and psoriasis (4.8%). A full list of diagnoses is provided in Supplemental Table I (available online at www.jaad.org).

Table IV. Results of multivariable analysis of the variables associated with adult female acne onset

Variable	OR* (95% CI)	*P* value
Constitutional factors		
History of acne in first-degree relatives		
Parents		
No	1	
Yes	3.02 (1.80-5.06)	<.001
Siblings		
No	1	
Yes	2.40 (1.46-3.94)	.001
Other general factors		
Present or last occupation		
None/housewife	1	
Student	1.09 (0.44-2.73)	.85
Unskilled worker	1.46 (0.63-3.40)	.38
Office worker	2.24 (1.24-4.06)	.007
Manager/freelance	0.82 (0.39-1.72)	.60
History of pregnancy		
No	1.71 (1.06-2.78)	.02
Yes (1+)	1	
History of adolescent acne		
No	1	<.001
Yes	5.44 (3.43-8.61)	
Comorbidities and stress		
Hirsutism		
No	1	
Yes	3.50 (1.42-8.60)	.006
Stress during last month		
No/mild	1	
Moderate	1.33 (0.76-2.30)	.32
High/very high	2.95 (1.57-5.53)	.001
Food intake (days/week)		
Fruits/vegetables		
≤3	2.33 (1.20-4.53)	.01
>3	1	
Fresh fish		
≤3	2.76 (1.31-5.81)	.008
>3	1	

CI, Confidence interval; *OR*, odds ratio.
*Multistage hierarchical multiple logistic regression with forward stepwise selection algorithm; age was included as a fixed adjustment factor in the models.

Medical histories

The subjects' medical histories, overall and stratified by case or control status, are shown in Table II. A history of acne during adolescence was reported in 68.1% of the cases compared with 28.5% of the controls ($P < .001$). A family history of acne was present in 42.7% of the women, with a significant between-group difference ($P < .001$), although this finding was relevant only for first-degree relatives (ie, parents and siblings). Regarding the presence of comorbidities, a diagnosis of PCOS or hirsutism was reported by 21.8% of women, and it was significantly associated, at the univariate level, with an increased risk of AFA. A total of 22.3% of the women reported having irregular menstrual patterns, and 24.2% reported using oral contraceptives, without any significant differences between the cases and controls. A total of 27.1% of the subjects reported having a high or very high level of stress during the last month, with an overall significant difference between the 2 groups ($P = .001$).

Food intake

Food intake frequency, overall and according to the case-control status, is shown in Table III. Regular milk consumption (>3 days/week) was recorded in 55.0% of the patients, without any significant difference in milk type between the cases and controls. In total, 51.1% of the women regularly ate dairy products, 83.8% consumed starchy foods, 39.3% ate cakes and sweets, 29.5% consumed chocolate, and 20.5% ate beef, without any significant between-group differences. The rate of women consuming vegetables and fruit or fish was significantly higher in the controls compared to the cases ($P = .02$ and $P = .05$, respectively).

Multivariable analysis

The multivariable analysis results of the variables associated with AFA in the univariate analysis are shown in Table IV. After adjusting for age, a history of acne in first-degree relatives—either parents (OR = 3.02 [95% CI, 1.80-5.06]) or siblings (OR = 2.40 [95% CI, 1.46-3.94])—was significantly associated with AFA. The following variables were also associated with AFA: being an office worker (OR = 2.24 [95% CI, 1.24-4.06]) compared to being unemployed or a housewife, having a personal history of acne during adolescence (OR = 5.44 [95% CI, 3.43-8.61]), having no previous pregnancies (OR = 1.71 [95% CI, 1.06-2.78]), having hirsutism (OR = 3.50 [95% CI, 1.42-8.60]), and having a high or very high level of reported psychological stress during the last month (OR = 2.95 [95% CI, 1.57-5.53]) compared to having no stress or a mild level of stress. Regarding food consumption, a low weekly intake (≤3 days/week) of fruits and vegetables (OR = 2.33 [95% CI, 1.20-4.53]) and consuming fresh fish (OR = 2.76 [95% CI, 1.31-5.81]), were associated with AFA after controlling for all other variables in our multivariate analysis. No additional associations emerged.

DISCUSSION

Few formal epidemiologic studies have evaluated risk factors for the presence of AFA. Our case-control study indicated that having a personal history of acne

in adolescence, a family history of acne in first-degree relatives, no previous pregnancies, having hirsutism, working as an office worker, reporting a higher level of psychological stress, and having some dietetic factors, including a low consumption of vegetables or fruit and fish, were all associated with AFA. We did not establish an onset date for acne, and our associations may not reflect a causative role but may, at least in part, reflect shared risk factors or consequences of established acne. The small proportion of patients (7%) with severe acne was consistent with previous results reported in the literature,[6] which often define AFA as a mild to moderate condition. A total of 75.2% of the patients had the inflammatory form of the disease rather than the retentional form. This finding aligned with data previously reported by Dréno et al.[11] Our data also confirmed that the face is the predominant area affected by AFA, with lesions mainly localized at the cheeks and chin, which indicates the propensity of this clinical variant to be localized in the middle and inferior areas of the face.[9] Truncal involvement was present in 30% of the cases. A history of acne in adolescence was reported by 68% of patients, indicating the predominance of a "persistent" AFA subtype compared to a "late onset" subtype, which aligns with the observations of other studies.[11] The mean age of the cases (32.2 years) was similar to that in previous reports,[12-14] confirming that AFA is primarily a young adult disease.

The association of acne with a family history of the disease, which we documented, confirms data from other studies that also indicated a stronger association with a history in parents compared to siblings.[3,10,11,13,15]

The association of AFA with hirsutism and having no previous pregnancies seems to support a connection between adult acne and hormonal factors, such as hyperandrogenism, even if the association between AFA and a history of PCOS was not confirmed in our multivariable analysis, possibly because of a limited statistical power to document such an association. We did not collect blood samples to assess hormone levels. Note that other studies have shown a weak association between AFA and underlying androgenic abnormalities.[11] In our AFA study, we did not confirm the association between acne and BMI, which we documented in adolescent acne,[10] where the association was much stronger in men compared with women. Interestingly, male (but not female) obesity is associated with hyperlipidemia, and high lipid levels have been associated with severe acne.[16] Another debated association is with tobacco smoking, which was not documented in our AFA study, contrary to other experiences in which the disease, especially the comedonal noninflammatory variant, was strongly correlated with tobacco; one study referred to the condition as "smoker's acne."[9] The choice of proper controls might explain the different results obtained.

In a previous case-control study, we highlighted the importance of dietary factors in acne occurring in adolescents. Acne was associated with a high consumption of milk and skimmed milk, and it was inversely correlated with the intake of fish.[10] In the present study, we did not confirm the association with milk, although a regular intake of fish and fruits or vegetables were protective factors for the disease, possibly because of the antioxidant properties of these foods.[17] These findings, together with the lack of an association with BMI, seem to indicate a different pathogenesis of AFA compared to adolescent acne, with a lower impact of metabolic factors.

High or very high levels of psychological stress during the month preceding the clinical examination were also associated with AFA. This association is intriguing. Information on stress was self-reported by the patients and influenced by their perceptions. More convincing evidence could be derived from prospective studies assessing stressful events at several time points in relation with acne. Recent studies have shown that adult patients with acne are characterized by both common psychiatric conditions and a tendency to somatization.[18] A high level of stress was also observed by Albuquerque et al,[19] who showed that women with AFA are more prone to suffer from psychiatric conditions (eg, somatization, depression, and anxiety),[19] for which a multidisciplinary approach would be required. The prevalence of active working women from 25 to 39 years of age was particularly high, and we observed an association between AFA and office-related work, which is difficult to explain and possibly related to the work environment (eg lighting, air conditioning, etc) or psychological factors.

Our study had some limitations. We did not establish an onset date for acne, and some of our associations may reflect consequences of established acne. The age of patients with AFA was significantly lower than those without such a diagnosis, but we made adjustment by age in the multivariable analysis. Controls were recruited for a variety of clinical conditions unrelated to AFA. They were matched with cases on the setting of observation (ie, outpatient service), to control for factors related with seeking medical advice and the degree of attention for their health conditions.

In conclusion, our case-control study is one of the few studies adopting a formal epidemiologic methodology to assess the risk factors for AFA in women ≥25 years of age. Our study indicated that having a history of acne in adolescence, a history of acne in first-degree relatives, no previous pregnancies, having hirsutism, working as an office worker, and reporting a higher level of psychological stress—along with some dietetic factors, including low consumption of vegetables or fruit and fish—were all associated with AFA. Some of our associations could be viewed as explorative and therefore require further confirmation by other studies.

REFERENCES

1. Krowchuk DP. Managing adolescent acne: a guide for pediatricians. *Pediatr Rev*. 2005;26:250-261.
2. Cunliffe WJ, Gould DJ. Prevalence of facial acne vulgaris in late adolescence and in adults. *Br Med J*. 1979;1:1109-1110.
3. Golden V, Clark SM, Cunliffe WJ. Post-adolescent acne: a review of clinical features. *Br J Dermatol*. 1997;136:66-70.
4. Poli F, Dreno B, Verschoore M. An epidemiological study of acne in female adults: results of a survey conducted in France. *J Eur Acad Dermatol Venereol*. 2001;15:541-545.
5. Perkins AC, Maglione J, Hillebrand GG, et al. Acne vulgaris in women: prevalence across the life span. *J Womens Health*. 2012;21:223-230.
6. Preneau S, Dreno B. Female acne - a different subtype of teenager acne? *J Eur Acad Dermatol Venereol*. 2012;26:277-282.
7. Schmitt JV, Masuda PY, Miot HA. Acne in women: clinical patterns in different age-groups. *An Bras Dermatol*. 2009;84:349-354.
8. Schäfer T, Nienhaus A, Vieluf D, et al. Epidemiology of acne in the general population: the risk of smoking. *Br J Dermatol*. 2001;145:100-104.
9. Capitanio B, Sinagra JL, Bordignon V, et al. Underestimated clinical features of postadolescent acne. *J Am Acad Dermatol*. 2010;63:782-788.
10. Di Landro A, Cazzaniga S, Parazzini F, 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;67:1129-1135.
11. Dréno B, Thiboutot D, Layton AM, et al. Large-scale international study enhances understanding of an emerging acne population: adult females. *J Eur Acad Dermatol Venereol*. 2015;29:1096-1106.
12. Shaw JC, White LE. Persistent acne in adult women. *Arch Dermatol*. 2001;137:1252-1253.
13. Dumont-Wallon G, Dreno B. Specificity of acne in women older than 25 years. *Presse Med*. 2008;37:585-591.
14. Williams C, Layton AM. Persistent acne in women: implications for the patient and for therapy. *Am J Clin Dermatol*. 2006;7:281-290.
15. Knaggs HE, Wood EJ, Rizer RL, et al. Post-adolescent acne. *Int J Cosmet Sci*. 2004;26:129-138.
16. Arora MK, Seth S, Dayal S. The relationship of lipid profile and menstrual cycle with acne vulgaris. *Clin Biochem*. 2010;43:1415-1420.
17. Skroza N, Tolino E, Semyonov L, et al. Mediterranean diet and familial dysmetabolism as factors influencing the development of acne. *Scand J Public Health*. 2012;40:466-474.
18. Gül Aİ, Çölgeçen E. Personality traits and common psychiatric conditions in adult patients with acne vulgaris. *Ann Dermatol*. 2015;27:48-52.
19. Albuquerque RG, Rocha MA, Bagatin E, et al. Could adult female acne be associated with modern life? *Arch Dermatol Res*. 2014;306:683-688.

Supplemental Table I. List of diagnoses in control patients

Diagnosis, n (%)	Controls (N = 270)
Pigmentary lesion screening	98 (36.3)
Warts	15 (5.6)
Unspecified dermatitis/eczema	14 (5.2)
Psoriasis	13 (4.8)
Basal cell carcinoma	10 (3.7)
Androgenetic alopecia	9 (3.3)
Allergic contact dermatitis	9 (3.3)
Mycosis/onychomycosis	8 (3.0)
Seborrheic dermatitis	7 (2.6)
Atopic dermatitis	6 (2.2)
Seborrheic keratosis	4 (1.5)
Sebaceous cyst	4 (1.5)
Skin biopsy/surgery	3 (1.1)
Melasma	3 (1.1)
Vitiligo	3 (1.1)
Vaginitis	3 (1.1)
Acne rosacea	2 (0.7)
Angioma	2 (0.7)
Condylomata	2 (0.7)
Rash	2 (0.7)
Lentigo	2 (0.7)
Papular lesions	2 (0.7)
Lichen planopilaris	2 (0.7)
Chronic urticaria	2 (0.7)
Pityriasis versicolor	2 (0.7)
Telogen effluvium	2 (0.7)
Dermatofibroma	2 (0.7)
Actinic keratosis	1 (0.4)
Pendulous fibroids	1 (0.4)
Folliculitis	1 (0.4)
Hidradenitis suppurativa	1 (0.4)
Syphilis	1 (0.4)
Melanoma	1 (0.4)
Molluscum contagiosum	1 (0.4)
Pyoderma	1 (0.4)
Pyoderma gangrenousum	1 (0.4)
Pemphigus	1 (0.4)
Pityriasis rosea	1 (0.4)
Pruritus	1 (0.4)
Purpura	1 (0.4)
Plantar callus	1 (0.4)
Tinea pedis	1 (0.4)
Burn	1 (0.4)
Other/unknown	23 (8.5)