



## Original Research

## Prepubertal acne: A retrospective study

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## ABSTRACT

**Background:** Acne vulgaris is a common skin disorder, but studies on the epidemiologic features of prepubertal acne are limited.

**Objectives:** The aim of this study was to determine the prevalence and severity of prepubertal acne and to identify factors influencing acne severity and poor response to treatment.

**Methods:** A retrospective study was conducted on 683 patients with acne from our database who visited the dermatology department of Nantes University hospital between October 2014 and May 2018. Patients of prepubertal acne (7–12 years) were included in this study.

**Results:** Of the 683 patients with acne, 24 (3.5%) had prepubertal acne. Prepubertal acne was more common in female patients (75%). Acne severity assessment showed that severe acne (Groupe Expert Acné global acne severity scale 4) was the most common form (33%), and mild and moderate forms (Global Evaluation Acne Group, global acne severity scales 2 and 3) accounted for 25% each. There was a high predominance of phylotype IA<sub>1</sub> of *Cutibacterium acnes* (belonging to CC18 subgroup). The analysis of patients' lifestyle and acne features identified three factors associated with an increased risk of poor response or resistance to acne treatment. Initially severe acne grading (grade 4) was the most strongly associated parameter ( $p < .028$ ), followed by regular milk consumption and taking other medications in addition to acne treatment ( $p < .049$  for each).

**Conclusion:** This study reported on prepubertal acne features and identified three factors associated with a high risk of treatment failure or relapse. Adequate and prompt treatment is needed in this subgroup of patients to minimize disease burden and prevent subsequent disease worsening.

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## Introduction

Acne is one of the most common skin disorders. It is a chronic inflammatory skin disease of the pilosebaceous follicles that generally affects adolescents, in whom the reported prevalence ranges between 70% and 87% (Dreno and Poli, 2003). The epidemiology of acne is currently changing, with an increasingly earlier onset seen in childhood (Park et al., 2015).

Prepubertal acne is defined by an onset between the ages of 7 and 12 years and typically appears before the onset of any other pubertal signs (Fig. 1). Its incidence has increased in recent years. There is a genetic predisposition, and the earlier onset of acne has been assumed to be associated with an earlier puberty onset as a result of normal adrenarche associated with adrenal gland maturation (Gendler et al., 2017).

Recently, many studies in adults and adolescents have identified various factors, including genetic and lifestyle factors, associated with acne pathogenesis, treatment failure, and a chronic or relapsing course. Even though these reports have provided valuable evidence, significant data on prepubertal acne frequency and main features are still lacking. In addition, because childhood acne may persist over years, early management may help minimize its impact on patients.

The aims of this study were to define the clinical profile of patients with prepubertal acne based on a retrospective analysis of a cohort of patients seen over 4 years, to determine the phylotype of *Cutibacterium acnes* (*C. acnes*) isolated from skin-swab samples and the frequency of markers of bacterial resistance in prepubertal acne isolates, and to identify risk factors for treatment failure.

## Methods

For each patient consulting for acne, a standardized file is routinely filled during the initial visit in our department, including

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Fig. 1. Inflammatory prepubertal acne.

Table 1

Characteristics of the study population (n = 24)

Characteristics	No.	%	p-value
Age, years (mean ± SD)	17.6 ± 7.5		.343
Sex			.115
Female	18	75	–
Male	6	25	–
Body mass index	19.6 ± 2.8		.99
Age of acne onset, years (mean ± SD)	10.8 ± 1.7		.17
Family history of acne	22	95.1	.52
Mother	12	34.1	–
Father	11	29.3	–
Siblings	13	31.7	–
Nutrition habits			
Consumption of milk	20	83.3	.64
Sweets	10	41.6	–
Triggers of acne	13	55.2	.49
Stress	12	50	–
Sun exposure	4	17.2	–
Menstruation	4	17.2	–
Sweets	1	3.4	–
Hormonal contraception	4	16.7	.13
Medication besides acne	6	25	.049
Location of acne			
Face	23	98.7	.252
Back	19	79.2	.228
Chest	10	41.7	.803
Acne lesions, mean			
Inflammatory	22	95.2	.126
Noninflammatory	19	79.2	.126
Nodular form	7	29.2	.732
Scars	8	33.3	.33
Groupe Expert Acné global acne severity scale			
1	1	4.1	–
2	6	25	–
3	6	25	–
4	8	33	.028
5	2	8.3	–

SD, standard deviation

demographic information including age, sex, Fitzpatrick skin type, and body mass index; patient's lifestyle (sporting activities, dietary habits including daily milk consumption, smoking, use of cosmetics); characteristics of the menstrual cycle in women; and history of acne (family acne history, disease onset, presence of aggravating factors, and treatment history).

Clinical data were also systematically collected at each visit, including body areas affected by the disease (face, neck, back, chest and upper limbs); acne lesion types and counts (including comedones, papules, pustules, cysts, nodules, and scars) using the acne lesion rating scale (Echelle de Cotation des Lésions d'Acné) and the Groupe Expert Acné (GEA) global acne severity scale (Dréno et al., 2011); and acne treatments and evolution.

The clinical files of 683 patients with acne from our database who visited the dermatology department of Nantes University hospital between October 2014 and May 2018 were retrospectively reviewed. Patients who reported a disease onset between the age of 7 and 12 years were considered to have prepubertal acne and were included in this study. Clinical data were collected from patients' medical files.

The sampling procedure and bacteriological testing methods (bacterial identification, antibiotic susceptibility testing, and molecular typing) used in this study have been previously described (Dagnelie et al., 2018). *C. acnes* strain populations are divided into six main phylotypes (IA<sub>1</sub>, IA<sub>2</sub>, IB, IC, II, and III) with the presence of subgroups among the phylotypes, identified according to genome analyses (multi- and single-locus sequence typing). These cluster differentiations are called clonal complexes (Dagnelie et al., 2018).

All statistical analyses were performed using SPSS Statistics version 19.0, and  $p < .05$  was considered statistically significant. A logistic regression analysis was used to identify potential risk factors for worsening acne. In the descriptive analysis, qualitative data are presented as absolute and relative frequencies. Quantitative data are presented as mean ± standard deviation. The normal distribution of variables was studied using the Kolmogorov–Smirnov test. In the bivariate analysis, qualitative variables were compared using a Pearson's Chi square or Fisher's statistical test if necessary. A Student's *t* test and Mann–Whitney test were used for categorical and quantitative variables.

## Results

Data from our acne outpatient database were retrospectively analyzed. Of the 683 patients with acne, 24 (3.5%) had prepubertal acne. Table 1 shows the patients' main characteristics. Prepubertal

acne was more common in female patients (25% of male and 75% of female patients). No association between sex and acne severity was identified.

The mean age of the study population was 17.6 years at the first visit. The mean age at acne onset was 10.8 years. All patients were Caucasian. The mean body mass index was 19.6 kg/m<sup>2</sup>, and most participants (91.6%) were in the normal weight category. The mean age of female patients at menarche was 12.3 years. A family history of acne was reported in 95.1% of patients. It involved the mother in 34.1% of patients and the father and brothers in 29.3% and 31.7% of patients, respectively.

None of the patients reported a smoking status. Six patients reported use of medications in addition to acne treatment (mainly proton pump inhibitors, antihistamines, and antidepressants). Also, 79.2% of patients did not use any contraception method. The most used contraception method was low-dose birth control pills (16.7%). Twenty-one patients practiced sports, most often indoor sports (51.9%) and less than three times per week (66.7%). At least one triggering or aggravating factor of acne was reported by 55.2% of patients (sun exposure in 17.2%, menstruation in 17.2%, and stress in 13.8%). Cosmetic care products were used by 61.1% of patients (mask or scrub).

Regarding acne treatment, 17.4% of patients were not treated. At least two successive treatments had been prescribed to more than half of the patients. Furthermore, 66.6% of patients had received local treatments, including benzoyl peroxide (54.1%), topical antibiotics (erythromycin in 29.2%), and topical retinoids (50%). Systemic approaches were used in 82.6% of patients, including zinc salts (17.4%), oral antibiotics (36.9%, including tetracycline in 15.2% and doxycycline in 21.7%), and oral isotretinoin (15.2%).

The face was the most commonly affected body site (98.7%), followed by the back (79.2%) and the chest (41.7%). In 95.2% of cases, inflammatory lesions were present (Fig. 1), with 79.2% of patients having comedonal acne and 29.2% a nodular form. Scars were reported in 63.6% of cases and were often atrophic (21.2%). Regarding acne severity, severe acne (GEA scale 4) was the most common form (33%), whereas mild and moderate forms (GEA scales 2 and 3) accounted for 25% each. No evidence of androgen excess or other clinical signs of virilization was found. Hormone levels were assessed in 20.8% of patients with acne, without any abnormality.

In seven patients, swab samples were taken from a surface area surrounding an inflammatory lesion. A culture positive for *C. acnes* was obtained for all patients, and 57.1% ( $n=4$ ) of strains were resistant to macrolides but remained sensitive to tetracycline. Two of the six main phylotypes were identified: IA<sub>1</sub> ( $n=5$ ) and IB ( $n=2$ ). Among the seven *C. acnes* strains, 4 belonged to CC18, 2 to CC36, and 1 to CC3. The five phylotype IA<sub>1</sub> strains belonged to SLST-types A1 ( $n=3$ ), A2 ( $n=1$ ), and C2 ( $n=1$ ), and both phylotype IB strains belonged to SLST-type H1 ( $n=2$ ).

Among the 24 patients identified, four were lost to follow-up. Follow-up data on treatment were collected an average of 14.2 months (range, 3–56 months) after the initial visit. Treatment failure (patients with grade  $\geq 3$  acne under treatment) was reported in 35% of patients, and 12.2% of patients experienced at least one relapse (increase by 2 grades; e.g., from grade 1 to 3), which was most often mild (41.7% with GEA scale 2 acne) or moderate (12.5% with GEA scale 3 acne).

The analysis of patients' lifestyle and acne features identified three factors associated with an increased risk of poor response or resistance to acne treatment: an initially severe GEA acne grading was the most strongly associated parameter ( $p < .028$ ), followed by regular milk consumption (at least 1 glass per day) and taking other medications in addition to acne treatment ( $p < .049$  for each). Patients with high milk consumption were at a higher risk of severe acne and treatment failure. The consumption was in most cases semi-skimmed milk (45.8%). No correlation was found between sweet food consumption and acne severity.

## Discussion

This study showed a prevalence of prepubertal acne of 3.5% in our population. Prepubertal acne mainly affected female patients and was severe and difficult to treat in most cases.

Acne is most often associated with adolescence but can be present at any age (Dreno and Poli, 2003). In previous decades, prepubertal patients with acne were thought to require a systematic endocrine evaluation due to prepubertal acne scarcity and potentially harmful nature (Que et al., 2016). Currently, prepubertal acne is considered a normal variant of acne that is not related to endocrine disorders in most cases (Mancini et al., 2011). In our cohort of 683 patients with acne, the prevalence of prepubertal-onset acne was 3.5%, a value that is similar to the prevalence of childhood acne of 1.8% to 3.9% previously reported in Taiwan (Yang et al., 2007).

In the paper by Davis et al. (2013), 55 million pediatric acne visits took place over a 6-year period, and preadolescent acne accounted for 4.8% of acne cases. Another prospective observational study conducted in Italy showed that acne prevalence was lowest in 9-year-old children (6%; Napolitano et al., 2018). In our study, female patients were more affected (75%) than male patients (25%), as previously reported (Napolitano et al., 2018). Several studies have identified a strong role of heredity in acne (Wolkenstein et al., 2018). Our study confirmed these results; 95% of our patients had a first-degree family history of acne (Dréno et al., 2016). We did not find any association between acne severity and family history of acne, unlike Ballanger et al. (2006).

Among the lifestyle factors investigated in our study, milk consumption was the only factor associated with an increased risk of treatment failure in the bivariate analysis. A retrospective recall-based study in adults and a prospective study in adolescent girls suggested an association between acne and the consumption of milk and other dairy products (Adebamowo et al., 2005; 2006). These two studies failed to identify a difference based on milk fat content. Conversely, Adebamowo et al. (2008) reported that only skimmed milk consumption significantly correlated with acne in teenage boys. In our study, the consumption of semi-skimmed milk was higher than skimmed milk (45.8%).

Psychosocial and lifestyle factors, including stress, emotions, sleep deprivation, and a modern lifestyle, could play a role in acne (Dréno et al., 2018a). In our study, 13.8% of patients reported stress-related worsening of acne. The relation between stress and acne worsening is now well established and is explained by a higher production of neuromodulators, such as the substance P, that stimulate sebum production by the sebaceous gland.

Systemic treatment for indications other than acne was associated with a poor response to treatment in the bivariate regression analysis ( $p < .049$ ). The multiplicity of treatments could decrease treatment adherence. Anderson et al. (2015) showed that switching from one treatment to several treatments decreased adherence.

Prepubertal acne is characterized by a predominance of comedones on the T-zone of the face, with relatively few inflammatory lesions (Shalita et al., 2011), as shown in a US study in which the prevalence of comedonal acne was 47% in children age  $<11$  years (Lucky et al., 1994). In our study, 95.2% of cases presented with inflammatory lesions, 79.2% had comedonal acne, and only 29.2% had a nodular form of acne. Early onset of comedonal acne could be predictive of a more severe form of the disease later. Appropriate and early treatment is particularly important to prevent unwanted sequelae in this population.

The face was the most commonly affected body site (98.7%); however, the trunk was more often affected in this population than in adults and teenagers, with 79.2% of acne lesions on the back and 41.7% on the chest. The evaluation of acne severity in our study showed that severe acne (GEA scale 4) was the most common form, found in 33% of cases. These results differ from those of Napolitano et al. (2018), who reported that 88.5% of examined children had mild or almost clear acne, suggesting that moderate-to-severe forms of the disease are very rare in the preadolescent age range. Our results are in accordance with a study that reported that experiencing a higher number of comedones or inflammatory lesions before puberty is associated with the subsequent development of severe acne (Lucky et al., 1997). Scars were found in 33.3% of prepubertal acne cases, confirming the severity of this form of acne and the need for early treatment.

Our study showed a high predominance of phylotype IA<sub>1</sub> (CC18), as described previously (Dagnelie et al., 2018; Lomholt et al., 2017). To our knowledge, this was the first study to describe bacteriological features in prepubertal acne. Dagnelie et al. (2018) found a significant association between SLST-type A1, identified in 3 patients, and severe back acne. Lomholt et al. (2017) also reported an association between CC18 and acne. *C. acnes* is generally sensitive to a broad range of widely used antimicrobials. However, resistance of *C. acnes* to antibiotics has emerged over the years, with high resistance rates reported for erythromycin (macrolides) and clindamycin (lincosamides; 21%–70%) and rarer resistances to tetracycline (4%–30%; Dréno et al., 2018b).

Patients with prepubertal acne are likely to develop more severe or sustained acne in adolescence or adulthood (Lucky et al., 1991). In our study, 12.2% of patients experienced at least one relapse and 35% did not respond to treatment.

## Conclusion

Our study showed that preadolescent acne is a rare disease, affecting only 3.5% of patients. Most patients had a severe form of the disease, and *C. acnes* phylotype IA<sub>1</sub> was identified in most tested patients. A resistance to macrolides was found in 57.1% of cases. The main risk factors identified for a poor response to treatment were a severe GEA acne grading at onset, milk consumption, and use of other medications in addition to acne treatment. However, adequate and prompt treatment is also needed in this subgroup of patients to minimize the disease burden and prevent possible worsening of the disease. Prepubertal patients with acne are a specific patient population that deserves further study.

## Conflicts of interest

None.

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None.

## Study approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

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