

## Attention Deficit Hyperactivity Disorder and Treatment Adherence in Adolescent Acne Patients: Investigating the Relationship for Better Care Strategies

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**ABSTRACT** **Introduction:** Accompanying comorbidities in acne vulgaris (AV) patients affect treatment adherence.

**Objectives:** The purpose of this study was to investigate the relationship between treatment compliance and attention deficit hyperactivity disorder (ADHD) in adolescents with AV.

**Methods:** This study included 140 patients with AV. At the beginning of the treatment, each patient acne severity was assessed, and the Connors-Wells Adolescent Self-Report Scale-Long Form (CASS-L) was administered. The Morisky Medication Adherence Scale (MMAS-8) was used to assess treatment adherence. The treatment response was assessed using a six-point scale.

**Results:** Significant differences were found in the scores on the 10 subscales of the CASS-L among the 3 groups. The Global Acne Grading System (GAGS) scores showed a positive correlation with the scores of the subscales of the CASS-L, with 3 of them at a moderate level and 7 at a weak level. Five MMAS subscales had a weak correlation and 5 had a moderate correlation with the CASS-L subscale scores. The 9 subscales and the treatment response showed a slight negative correlation.

**Conclusions:** ADHD is one of the many psychiatric comorbidities that frequently coexist with acne vulgaris. Its treatment is long-term and achieving a good treatment response relies heavily on patient adherence. Our study, which showed a decrease in acne treatment adherence and response as ADHD symptoms increased, will raise awareness among dermatologists to be more vigilant in their approach to this patient group.

## Introduction

Acne vulgaris (AV) is a chronic inflammatory condition that is commonly observed in adolescents and adults. Its etio-pathogenesis involves abnormal follicular hyperkeratinization, hyperseborrhea, colonization by *Cutibacterium acnes*, and inflammation. Furthermore, it is commonly known that androgens play a role in the occurrence of acne [1,2]. Androgens increase sebum secretion and keratinocyte proliferation, leading to increased bacterial colonization and inflammation [1].

The neurodevelopmental disorder known as Attention Deficit Hyperactivity Disorder (ADHD) is defined by impulsivity, hyperactivity, and inattention. While the exact cause of it is unknown, a number of variables, including stress, hormones, and heredity, are thought to be involved. There is a correlation between ADHD and higher incidence of other psychiatric comorbidities [3]. Research on individuals with acne vulgaris suggests increased prevalence of diverse psychiatric disorders [4].

## Objectives

To our knowledge, psychiatric comorbidities accompanying acne reduce patients treatment adherence [5]. Moreover, ADHD can trigger the emergence of various psychiatric comorbidities in patients with acne [6]. Clinical studies have investigated psychiatric comorbidities and treatment adherence in patients with acne vulgaris [5,7–10]. Still, no clinical study that we are aware of has looked into how ADHD affects treatment response and adherence for acne. Our goal was to look into these associations in teenage AV patients who also exhibit symptoms of ADHD.

## Methods

### Study Design

Between October 25, 2023, and April 25, 2024, 140 volunteer acne vulgaris patients aged 12-17 who visited the dermatology outpatient clinic were included in the study. Since the patients were under 18 years old, informed consents were obtained from their parents. Individuals aged >18 years with neurological/systemic diseases or chronic

medication use were excluded from this study. The patients who participated in the study applied to the outpatient clinic with their parents before treatment and at each follow-up visit. Information about the drugs prescribed for treatment and the use of these drugs was explained to both the patient and his/her parents. Especially in younger patients, it was ensured that the treatment was carried out under parental control. During the initial examination, sociodemographic data were collected. Global Acne Grading System (GAGS) and type of treatment decided after the examination (topical medication, topical and oral medication, or oral isotretinoin) were recorded. Each patient was then administered the Conners-Wells Adolescent Self-Report Scale-Long Form (CASS-L).

At the 12-week follow-up, a 6-point scale for treatment response and the Morisky Medication Adherence Scale (MMAS) for treatment adherence were applied. Patients were categorized into 3 groups according to MMAS: high, moderate, and low adherence. The CASS-L scores and treatment methods were compared between the groups. The correlations between CASS-L scores and acne severity (GAGS), treatment adherence (MMAS), and treatment response were examined.

The Giresun Training and Research Hospital Clinical Research Ethics Committee (19.06.2023/17) granted ethical approval for this study.

### Global Acne Grading System

In 1997, the Global Acne Grading System (GAGS) was first created. Using a scale of 0 to 4, the severity in each region of the face, chest, and back is assessed (0 indicating no lesions, 1 for comedones, 2 for papules, 3 for pustules, and 4 for nodules). Each anatomical region factor was established by taking into account the density, distribution, and surface area of the pilosebaceous units. After computing the overall score for every six areas, the severity of the acne was divided into four categories: mild (1–18), moderate (19–30), severe (31–38), and very severe (>39) [11].

### Conners-Wells Adolescent Self-Report Scale-Long Form (CASS-L)

Adolescent psychopathology, specifically ADHD, is measured in adolescents between the ages of 12 and 17 using

the Conners-Wells Adolescent Self-Report Scale (CASS-L). It relies on adolescents reflections on their experiences in the past month. The CASS-L consists of 87 items and includes 10 subscales: family problems, emotional problems, conduct problems, cognitive problems/attentiveness, anger control problems, hyperactivity, ADHD index, and the Diagnostic and Statistical Manual of Mental Disorders (DSM) Symptom Scales (DSM-IV-Inattentive, DSM-IV-Hyperactive-Impulsive, and DSM-IV-Total). The higher the score on the scale, the more the adolescent has a problem defined by the scale. The validity and reliability of the CASS-L has been established for Turkish patients, demonstrating the suitability of its psychometric properties for research purposes [12]. In this study, this scale was used to determine the severity of ADHD symptoms.

### Scale of Acne Severity Based on Percentage of Reduction (SASBR)

Christiansen et al created a scale in 1977 that uses the percentage of reduction to determine how severe acne is. This scale categorizes treatment effectiveness into the following six levels: A score of 4 indicated a 100% reduction in acne lesions, indicating excellent results. A score of 3 indicates a 75%–99% reduction, which is considered good. A score of 2 signifies a 50%–74% reduction, classified as moderate. A score of 1 represents a 1%–49% reduction, which is deemed insufficient. A score of 0 indicates no change in acne severity, while a score of -1 signifies a worsening condition. This scale provides a clear and objective way to evaluate the success of acne treatment and guide adjustments in treatment plans, as needed [13].

### Morisky Medication Adherence Scale

In 1986, Morisky et al created the MMAS-8 to measure medication adherence in people with long-term conditions. Originally composed of four questions, the scale was later revised to include eight. The MMAS-8 consists of seven dichotomous (yes/no) questions and a five-point Likert scale. A “no” response receives one point for questions 1-4, 6, 7, and a “yes” response receives one point for question 5. The eighth question, a Likert-type question, was scored with 1 point for “never/rarely” and 0 points for all other responses. A total score of 8 indicated high adherence, 6-7 indicates medium adherence, and a score of less than 6 indicated low adherence. The scale has undergone validity and reliability tests [14]. As an example, a pre- and post-treatment photograph of a patient with high adherence to treatment is presented in Figure 1.

### Statistical Analysis

Data were analyzed using the statistical program SPSS version 25.0. For categorical data, descriptive statistics are



**Figure 1.** Pre-treatment (GAGS:25) and 3-month follow up photograph (SASBR:4, MMAS:8) of the 16 years old patient receiving oral isotretinoin.

displayed as numbers and percentages; for numerical data, they are displayed as mean, standard deviation, minimum, and maximum. The categorical variables were compared based on treatment adherence using the chi-square test. Once the Kolmogorov-Smirnov test had determined whether the numerical variables were normally distributed, the Kruskal-Wallis test was employed to compare the data in terms of treatment adherence. The significance level was set at  $P < 0.05$ , and 95% confidence intervals (CI) were calculated.

## Results

The study comprised 140 AV patients who were monitored for 3 months in total. Treatment adherence of the patients was assessed using the MMAS-8, and based on this, they were categorized into 3 groups: high adherence, medium adherence, and low adherence. Among the group with low adherence, 26.7% had mild, 51.1% had moderate, and 22.2% had severe acne. In the medium adherence group, 62.5% had mild acne and 37.5% had moderate acne. In the high adherence group, 63.8% had mild acne and 36.2% had moderate acne. The groups did not differ statistically significantly with regard to age, sex, or length of acne. Only the topical treatment showed a significant difference ( $P = 0.008$ ). Comparing the medium- and high-adherence groups to the low-adherence group, the rates of topical treatment use were higher. However, no significant difference was observed between the groups in terms of specific topical treatment agents (Table 1).

The CASS-L subscale scores of patients with low, medium, and high adherence to acne vulgaris treatment were

**Table 1. Distribution of Study Variables Across Groups Based on Treatment Adherence**

Characteristics	Low Adherence N = 45 (%)	Medium Adherence N = 48 (%)	High Adherence N = 47 (%)	P Value
Age (years) mean ± SD	15.11 ± 1.66	15.35 ± 1.45	15.47 ± 1.38	0.740
Sex				0.734
Male	14 (31.1%)	18 (37.5%)	18 (38.3%)	
Female	31 (68.9%)	30 (62.5%)	29 (61.7%)	
Acne duration (month)	21.24 ± 16.88	21.50 ± 14.0	22.11 ± 16.11	0.332
Topical medication	9 (20%)	23 (47.9%)	22 (46.8%)	0.008
Topical retinoids	4	10	8	0.273
Benzoyl peroxide and antibiotic combination	5	13	14	0.071
Topical medication and oral antibiotic	19 (42.2%)	13 (27.1%)	14 (29.8%)	0.257
Oral isotretinoin	17 (37.8%)	12 (25%)	11 (23.4%)	0.249

SD = standard deviation.

**Table 2. Comparison of CASS-L Subscale Scores Across Groups Based on Treatment Adherence**

CASS-L Subscales	Low Adherence N = 45 (mean)	Medium Adherence N = 48 (mean)	High Adherence N = 47 (mean)	$\chi^2$	df	P Value
CASS-L–Family Problems	86.46	68.07	57.70	11.864	2	0.003
CASS-L–Emotional Problems	92.01	66.83	53.65	21.242	2	0.000
CASS-L–Conduct Problems	82.81	74.24	54.89	11.812	2	0.003
CASS-L–Cognitive Problems/Inattentive	90.56	69.79	52.02	20.876	2	0.000
CASS-L–Anger Control Problems	87.23	73.46	51.46	18.345	2	0.000
CASS-L–Hyperactivity	87.14	71.00	54.05	15.416	2	0.000
CASS-L–ADHD Index	92.84	65.88	53.83	22.305	2	0.000
CASS-L–DSM-IV-Inattentive	94.73	68.67	49.17	29.337	2	0.000
CASS-L–DSM-IV-Hyperactive/Impulsive	92.18	69.51	47.40	24.338	2	0.000
CASS-L–DSM-IV-Total	95.68	69.51	47.40	32.688	2	0.000

CASS-L = Conners-Wells Adolescent Self-Report Scale-Long Form; DSM = Diagnostic and Statistical Manual of Mental Disorders.

compared. Significant differences were observed for all ten subscales ( $P < 0.05$ ). As the CASS-L subscale scores increased, indicating an increase in ADHD symptoms, treatment adherence also decreased (Table 2).

Correlations between CASS-L subscale scores and acne severity, treatment adherence, and treatment response scores

were analyzed. The results of the Spearman rho correlation test, as detailed in Table 3, revealed significant relationships between various CASS-L subscale scores and measures of GAGS, MMAS-8, and treatment response. Specifically, there is a positive correlation with GAGS and negative correlations with MMAS-8 and treatment response.

**Table 3. Correlations Between CASS-L Subscale Scores and Acne Severity, Treatment Adherence, and Treatment Response Scores**

CASS-L Subscales	GAGS <sup>a</sup>	MMAS-8 <sup>a</sup>	Treatment Response
CASS-L– Family Problems	r : 0.386 P = 0.000	r : -0.323 P = 0.000	r : -0.312 P = 0.000
CASS-L– Emotional Problems	r: 0.413 P = 0.000	r : -0.416 P = 0.000	r : -0.249 P = 0.003
CASS-L– Conduct Problems	r: 0.328 P = 0.000	r : -0.314 P = 0.000	r : -0.317 P = 0.000
CASS-L– Cognitive Problems/Inattentive	r: 0.365 P = 0.000	r : -0.383 P = 0.000	r : -0.112 P = 0.187
CASS-L– Anger Control Problems	r: 0.317 P = 0.000	r : -0.394 P = 0.000	r : -0.314 P = 0.000
CASS-L– Hyperactivity	r: 0.366 P = 0.000	r : -0.365 P = 0.000	r : -0.238 P = 0.005
CASS-L– ADHD Index	r: 0.436 P = 0.000	r : -0.400 P = 0.000	r : -0.279 P = 0.001
CASS-L– DSM-IV-Inattentive	r: 0.391 P = 0.000	r : -0.468 P = 0.000	r : -0.237 P = 0.005
CASS-L– DSM-IV-Hyperactive/Impulsive	r: 0.361 P = 0.000	r : -0.430 P = 0.000	r : -0.242 P = 0.004
CASS-L– DSM-IV-Total	r: 0.411 P = 0.000	r : -0.494 P = 0.000	r : -0.278 P = 0.001

<sup>a</sup> Spearman rho correlation test.

Note: ‘r’ represents the strength and direction of the association between two variables. An ‘r’ value between 0.00-0.19 indicates a very weak correlation, 0.20-0.39 indicates a weak correlation, 0.40-0.69 indicates a moderate correlation, 0.70-0.89 indicates a strong correlation, and 0.90-1.00 indicates a very strong correlation. CASS-L = Conners-Wells Adolescent Self-Report Scale-Long Form; DSM = Diagnostic and Statistical Manual of Mental Disorders; GAGS = Global Acne Grading System; MMAS-8 = Morisky Medication Adherence Scale.

## Conclusions

Treatments for AV can have a variety of negative effects from topical to systemic. Topical treatment can cause peeling, burning sensation, dryness, erythema, scaling, and pain. Among systemic treatments, antibiotics, such as doxycycline, can cause gastrointestinal side effects, such as phototoxicity, nausea, vomiting, and esophagitis. Another systemic treatment option, isotretinoin, can lead to mucocutaneous, musculoskeletal, and ophthalmic disorders as well as changes in liver function tests and blood lipid profiles. These side effects often limit their use. Additionally, some patients may be prescribed combinations of topical and systemic treatments, complicating medication regimens and disrupting adherence. However, to observe the effects of AV medications, they should be used regularly for an average of 12 weeks [15]. Therefore, treatment adherence is crucial for success [16].

The degree to which a patient adheres to the recommended course of treatment is referred to as treatment adherence. Non-adherence can be classified as primary (failing to

obtain and start treatment) or secondary (not following the treatment procedure or discontinuing the treatment). While the acceptable rate of treatment adherence is 80%-95%, it is typically approximately 50% for most chronic diseases. Non-adherence to treatment remains a significant issue, especially in chronic diseases, such as acne vulgaris [17,18].

Many previous studies have investigated treatment adherence in patients with AV [10,16,17,19]. The adherence rates in these studies varied widely, from 7% to 96% [10]. We believe that this wide range was due to the different methodological approaches used to assess treatment adherence. In our study, we used the validated MMAS-8 to measure it. Three groups were created based on the MMAS-8. The distribution of patients receiving only topical treatment showed a significant difference, despite the fact that there were no statistically important differences between groups in regarding age, gender, or length of acne. In the medium- and high-adherence groups, the proportion of patients receiving only topical treatment was higher than that in the other treatment options (P = 0.008).

Diverse outcomes have been reported in prior research examining the adherence of patients receiving topical treatment for acne vulgaris. Some studies have reported increased adherence to topical treatment, which is consistent with our findings. For instance, Dreno et al found higher adherence among those receiving only topical treatment compared to those receiving both topical and systemic treatments, or isotretinoin, noting that adherence increased if the topical treatment was applied once daily, had fewer side effects, and had a rapid onset of action [20]. Similarly, in a study including 428 patients, Miyachi et al observed higher adherence among patients with acne receiving topical treatment, highlighting that adherence was influenced by treatment satisfaction and side effects [21]. Conversely, while some studies have found lower adherence rates among patients receiving topical treatment, others have indicated that adherence does not decrease with topical treatment [10–19]. Kouotou et al found higher adherence in patients receiving oral treatment than in those receiving topical treatment. Conducted in Africa, this study suggested that patient higher sociocultural beliefs in systemic treatments could lead to greater treatment satisfaction, and thus, higher adherence [19]. Similarly, Hayran et al observed that patients using both topical medication and oral antibiotics had higher treatment adherence than those using only topical treatments. Despite the known decrease in adherence to complex treatment regimens, it was suggested that increased patient satisfaction might have improved adherence [10].

It has been shown that patients with AV have higher rates of various psychiatric comorbidities such as depression, anxiety, stress, and increased suicide risk than healthy controls [4]. ADHD can also trigger various psychiatric morbidities in these patients [6]. In studies evaluating patients with AV, the factors that reduce treatment adherence include lack of information, difficulties in using medications, poor doctor-patient relationships, side effects, cost, and psychiatric comorbidities [22,23]. Psychiatric diseases can lead to a decrease in patients beliefs about the effectiveness and success of treatment, resulting in dissatisfaction, inadequate treatment, or refusal of treatment [4].

Research has indicated that psychiatric disorders reduce treatment adherence in patients with acne [9,19,24]. The MMAS, which we also utilized in our study, was utilized by Kouotou et al to assess acne patients compliance to treatment. They observed that over 50% of the patients had low treatment adherence, and psychiatric comorbidities were identified as contributing factors. They thought that those with psychiatric disorders might not fully understand their illnesses and treatments and could forget to take their medications [19]. Renzi et al looked into the connection between psychiatric morbidity and treatment adherence in patients

with dermatological conditions, including those who had AV. Patients with psychiatric comorbidities such as anxiety and depressive disorders were found to have low treatment adherence. Psychiatric comorbidities were identified as the most important reason for treatment non-adherence [24]. In 204 patients with AV, Alghofaili et al looked into the effect of depression on treatment compliance and discovered a negative correlation between treatment satisfaction and depression. Their results demonstrated that when satisfaction got higher, so did treatment adherence. Consequently, it was indicated that depression might coexist in patients with acne and that treating depression could enhance adherence to acne treatment [9].

Various research studies have examined children and teenagers compliance with ADHD medication; results have varied from 21%-74% [25–27]. Wehmeier et al noted that comorbidities, such as anxiety disorders, in children with ADHD also reduced treatment adherence [26]. All studies indicated that patient adherence decreased as the treatment duration increased. In adolescents, belief in the effectiveness of the drug increased their willingness to use it. The most important factors affecting medication adherence were effectiveness, tolerability, ease of use, simplified dosing regimen, cost, comorbid conditions, and frequency of doctor visits [25,27,28]. Our study was planned based on studies in the literature showing that treatment adherence in patients with AV or ADHD can decrease due to complex treatment regimens, low tolerance to adverse side effects, and prolonged treatment duration [27–29]. Consistent with this information, we found that patients with acne in the low treatment adherence group had more ADHD symptoms. Moreover, the correlation evaluation showed that as CASS-L scores increased, indicating the prevalence of ADHD symptoms, treatment adherence decreased.

## Limitations

Our study has a few limitations. First, the number of patients available for research was limited, which may affect how broadly the results can be applied. Second, the tools we use, such as the MMAS and CASS-L, rely on patients own assessments of their behavior and symptoms. These limitations highlight the need for further research to verify our findings.

A patient quality of life is greatly impacted by the chronic condition acne vulgaris. It is often associated with various psychiatric comorbidities, including ADHD. The side effects of medications used in AV treatment, need for prolonged therapy, and concurrent comorbidities can reduce treatment adherence. Enhancing adherence to treatment can result in better treatment outcomes, a higher standard of living, and lower expenses. Therefore, early detection and appropriate

management of psychiatric comorbidities such as ADHD in children and adolescents suffer from AV are crucial. Recognizing these conditions by dermatologists and referring relevant patients to child and adolescent psychiatric outpatient clinics can have positive implications for individuals health and quality of life.

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