Journal of Pioneering Medical Sciences
Received: March 25, 2026 | Accepted: October 24, 2026 | Published: November 05, 2026
Volume 15, Issue 10, Pages 324-333

DOI https://doi.org/10.47310/jpms2026151027



Acne Vulgaris Relapse After Oral Isotretinoin Therapy and Associated Factors in Al-Baha Province, Saudi Arabia: A Retrospective Cohort Study

Hasan S. AL-Ghamdi[1*], Mohammad A. Alghamdi[2], Reem Marzouq Alharthi[3], Faris Mohammed Alabdulmuhsin[4], Mohammed Saeed Alghamdi[5], Sara Mahfoud Alghamdi[6], Hanan Mesfer Alghamdi[7], Ahmed Saleh Alghamdi[8], Fatemah Hussain Algafli[9] and Ali Mohammed Alabdulmuhsin[10]

[1,2]Department of Internal Medicine, Division of Dermatology, Faculty of Medicine, Al-Baha University, Al-Baha City, Saudi Arabia
[3]Faculty of Medicine, Al-Baha University, Al-Baha, Saudi Arabia
[4]Department of Internal Medicine, Al-Ahsa Healthcare Cluster, King Fahad Hospital Hofuf, Hofuf, Saudi Arabia
[5]Department of Pediatrics, Al-Baha Healthcare Cluster, King Fahad Hospital Al-Baha, Al-Baha, Saudi Arabia
[6]Department of Dermatology, Al-Baha Health Cluster, King Fahad Hospital Al-Baha, Al-Baha, Saudi Arabia
[7]Department of Family Medicine, Al-Baha Health Cluster, Al-Baha, Saudi Arabia
[8]Al-Baha Health Cluster, King Fahad Hospital Al-Baha, Al-Baha, Saudi Arabia
[9]Department of Family Medicine, Al-Ahsa Health Cluster, Al-Ahsa, Saudi Arabia
[10]Faculty of Medicine, King Faisal University, Al-Ahsa, Saudi Arabia

Author Designation: [1,2]Associate Professor, [3,7,8,9]Medical Intern, [4]Resident R1, [5]Pediatrics Resident, [6]General Physician, [10]Medical Student

*Corresponding author: Dr. Hasan S. AL-Ghamdi (e-mail: H.saeed@bu.edu.sa).

©2026 the Author(s). This is an open access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0

Abstract **Background:** Oral isotretinoin is an effective systemic treatment for moderate-to-severe acne vulgaris; however, recurrence after treatment completion remains a concern in clinical practice. **Objective:** This study estimated the proportion of treatment completers reporting acne relapse after isotretinoin therapy and, secondarily, explored unadjusted associations between relapse and patient-related, clinical, treatment-related and adverse-effect factors in Al-Baha Province, Saudi Arabia. **Methods:** In this retrospective cohort study, patients prescribed oral isotretinoin at Prince Mishari Bin Saud Hospital between January and December 2024 were identified. Data were obtained from medical records and a one-time post-treatment interview using a structured questionnaire covering sociodemographic characteristics, acne features, family history, smoking status, body mass index, diet, treatment course, cumulative dose, treatment duration, adverse effects and patient-reported relapse after treatment completion. Post-treatment follow-up varied among participants, ranging from 6 to 18 months. **Results:** Of the 205 patients assessed, 116 completed therapy and were analyzed. Women accounted for 71.6% of participants and the mean age was 23±4.3 years. Relapse was reported by 49 of 116 treatment completers (42.2%). Among relapsed patients, 36 (73.5%) described the recurrence as less severe than at baseline and 32 (65.3%) experienced relapse within 12 months. The relapse rate decreased numerically across increasing cumulative-dose categories: ≤70 mg/kg, 18/39 (46.2%); 71-100 mg/kg, 12/27 (44.4%); 101-120 mg/kg, 8/20 (40.0%); and 121-150 mg/kg, 11/30 (36.7%). Relapse occurred in 41 of 83 females (49.4%) and 8 of 33 males (24.2%). Dry lips (92.2%), dry skin (83.6%) and dry eyes (75.9%) were the most common adverse effects. In an exploratory, unadjusted comparison, joint pain was reported in 53.1% of patients with relapse versus 32.8% of those without relapse (p = 0.029). **Conclusion:** These findings indicate that relapse was common among treatment completers, although most relapses were milder than baseline. Individualized dosing, adverse-effect management, maintenance therapy when indicated and structured follow-up are recommended. Larger prospective studies with standardized relapse definitions, longer follow-up, adherence assessment, hormonal evaluation and maintenance-therapy data are needed to clarify factors associated with relapse and inform relapse-prevention strategies for high-risk patients, particularly during the post-treatment follow-up period.

Key Words Acne Vulgaris, Isotretinoin, Acne Relapse, Recurrence, Cumulative Dose, Adverse Effects, Al-Baha, Saudi Arabia

INTRODUCTION

Acne vulgaris is a common inflammatory disease of the pilosebaceous unit that predominantly affects adolescents and young adults, although it may persist into adulthood or develop later in life. Its impact extends beyond cutaneous lesions; facial acne can affect self-image, confidence, social interactions, emotional well-being and overall quality of life [1]. Globally, acne remains one of the most common

dermatological conditions, although prevalence estimates vary by age, population and setting [2]. In Saudi Arabia, acne has also been reported frequently among young people, including those living in the Al-Baha Region [3]. Other Saudi studies have documented acne in community and university populations and examined acne-related knowledge, treatment practices, satisfaction and psychosocial health [4-6].

The psychological effects of acne are clinically important. Visible lesions may lead to embarrassment, anxiety, reduced self-esteem and avoidance of social situations. Studies conducted in Saudi Arabia have documented varying levels of quality-of-life impairment among young people with acne [7]. Accordingly, acne management should address lesion burden, scarring prevention and patient well-being, particularly in moderate-to-severe, persistent, scarring or treatment-resistant cases.

Treatment decisions are generally guided by acne severity, lesion morphology, affected sites, risk of scarring, previous treatment response, patient preference and reproductive considerations. Current guidelines recommend topical therapies, systemic antibiotics, hormonal therapy for selected female patients and oral isotretinoin for severe, nodular, scarring, refractory or psychologically distressing acne [8,9]. Oral isotretinoin is considered the most effective systemic therapy because it acts on several key pathogenic mechanisms, including sebaceous gland activity, abnormal follicular keratinization, *Cutibacterium acnes* proliferation and inflammation [10].

Although isotretinoin is highly effective, treatment requires individualized clinical planning. Clinical response and subsequent recurrence may be influenced by daily dose, cumulative dose, treatment duration, adherence, baseline severity, age, sex, seborrhea, hormonal factors and family history [11]. Clinicians must consider sustained acne control, treatment tolerability, laboratory and clinical monitoring, pregnancy-prevention counseling when appropriate and patient adherence [12]. A cumulative exposure of approximately 120-150 mg/kg has traditionally been recommended, although lower-dose approaches are also used to improve tolerability. Recent studies have examined whether cumulative dose, daily dose or continuation of treatment after lesion clearance is more important in reducing relapse and the need for retreatment [13]. The cumulative-dose categories used in the present study cannot establish the efficacy of the traditional target because treatment duration, adherence, clearance at treatment completion and maintenance therapy were not adequately controlled.

Adverse-effect management is integral to isotretinoin therapy. Cheilitis, xerosis and ocular dryness are common, whereas musculoskeletal symptoms, hair shedding, headache, mood-related symptoms and laboratory abnormalities may also occur. Previous reviews indicate that adverse events are common but generally manageable with appropriate counseling, dose adjustment when needed and monitoring [14,15]. In Saudi Arabia, patient knowledge regarding isotretinoin indications, teratogenicity, adverse effects, monitoring requirements and safe use varies, particularly among female patients [16,17].

Despite isotretinoin's ability to induce prolonged remission, acne recurrence after treatment completion remains an important clinical concern. Relapse may require topical maintenance therapy, additional systemic treatment, hormonal evaluation in selected cases or another course of isotretinoin. To the best of our knowledge, the frequency and severity of acne relapse after oral isotretinoin therapy, as well as potential factors associated with relapse, have not been specifically evaluated in Al-Baha Province. Therefore, the primary objective of this study was to estimate the proportion of treatment completers reporting acne relapse after oral isotretinoin therapy and, secondarily, to explore unadjusted associations between relapse and sociodemographic, clinical, treatment-related and adverse-effect factors among patients treated at Prince Mishari Bin Saud Hospital.

Regional relapse data are important because prescribing practices, medication availability, follow-up patterns and patient awareness may vary across regions. Reporting relapse frequency, timing, severity, cumulative-dose patterns and sex-specific proportions may inform realistic patient counseling and help identify patients who may benefit from closer follow-up after treatment completion.

METHODS

Study Design and Setting

This retrospective cohort study included patients with acne vulgaris who received oral isotretinoin at Prince Mishari Bin Saud Hospital (PMSH) in Al-Baha Province, Saudi Arabia. Data were extracted from hospital records and supplemented by a one-time post-treatment interview conducted after therapy completion. Relapse ascertainment relied partly on patient recall during the post-treatment interview, with medical records used to corroborate reports when available. The period for cohort identification and treatment initiation was January-December 2024, whereas treatment completion occurred between May 2024 and December 2025. The primary objective was to estimate the proportion of treatment completers reporting relapse after completion of isotretinoin therapy; the secondary objective was to explore unadjusted associations between relapse and patient characteristics, treatment exposure and reported adverse effects in routine dermatology practice.

The study was conducted in the Dermatology Department of PMSH, a referral hospital in Al-Baha Province, southwestern Saudi Arabia. The target population consisted of patients with acne vulgaris who were prescribed oral isotretinoin during the study period.

Study Population and Eligibility

The 205 patients initially assessed were identified consecutively from hospital records of oral isotretinoin

prescriptions issued between January and December 2024. Records for all 205 identified patients were available for assessment and no additional exclusions occurred beyond the 89 documented cases of treatment non-completion. Patients were eligible if they were 18-40 years of age, had acne vulgaris and received a prescription for oral isotretinoin during 2024. Patients were excluded if they were younger than 18 years, older than 40 years, declined participation or did not complete the prescribed treatment course. Treatment completion was determined from hospital medical records documenting completion of the prescribed isotretinoin course. Patients who stopped treatment before completing that course, including those who stopped after acne improvement, were categorized as non-completers. Consequently, 89 non-completers were excluded and 116 treatment completers were included in the final analysis. All 116 participants included in the final analysis were aged 18 years or older.

Sample-Size Determination

A formal sample size calculation was not performed because all eligible treatment completers during the study period were included. Accordingly, the analysis focused on relapse after treatment completion rather than on outcomes among all patients who were assessed or initiated treatment.

Data Collection

A structured questionnaire was developed from relevant literature and evaluated by dermatology consultants and academic experts. The questionnaire was pilot-tested before data collection, its Arabic-language wording was standardized and interviewers were trained to administer the questions consistently. Medical records provided isotretinoin start and end dates, prescribed and cumulative doses, treatment duration and completion status, clinical improvement, follow-up information, relapse status and severity and adverse effects. Cumulative isotretinoin dose (mg/kg) was calculated by dividing the total isotretinoin dose prescribed during treatment (mg), as recorded in hospital records, by baseline body weight (kg) at treatment initiation. Post-treatment interviews supplemented incomplete demographic, clinical, behavioral, treatment-related and relapse information. Because detailed adherence information was not consistently available, missed doses and temporary dose interruptions could not be reliably evaluated across the cohort. Recorded treatment completion was therefore not interpreted as confirmation of uninterrupted dosing or independently verified adherence. Post-treatment interviews and assessments were conducted from November 2025 to June 2026; follow-up data were included through June 30, 2026. Post-treatment follow-up varied among participants, with a documented range of 6-18 months. Individual follow-up durations could not be recovered for further analysis. Time to relapse was assessed from the date of isotretinoin treatment completion using medical-record documentation, supplemented by patient-reported information during post-treatment interviews when exact relapse dates were unavailable. Relapse timing was classified into three mutually exclusive categories: Less than 6 months, 6-12 months (inclusive) and more than 12 months after treatment completion.

The questionnaire covered four domains: sociodemographic characteristics; potential risk factors (smoking, family history and diet); treatment history (number of courses, daily and cumulative doses, duration and completion status); and relapse timing, site, severity and adverse effects. Daily-dose information was collected and cumulative dose was used in the reported treatment-dose analyses. Consumption of milk, high-fat meals or chocolate before and during isotretinoin treatment was summarized as a single yes/no measure of overall dietary exposure, rather than as separate food-specific variables. Accordingly, this measure describes combined dietary exposure and cannot isolate the association between any individual dietary factor and relapse.

Study Outcomes and Explanatory Variables

The primary outcome was acne relapse after completion of isotretinoin therapy. Relapse was defined as recurrence after evident improvement or clearance if the recurrence required prescription treatment or a second course of isotretinoin. In this study, "recurrence" denotes the return of acne after treatment, whereas "relapse" refers specifically to recurrence meeting this treatment-requiring criterion. Improvement or clearance following isotretinoin treatment was determined from the treating dermatologist's clinical documentation and supplemented by patient reports during the post-treatment interview. No standardized acne severity grading scale was used to quantify improvement or clearance. Relapse status was initially reported during the post-treatment interview. All 49 reported relapses met the treatment-requiring criterion and medical records documenting relapse or subsequent treatment were available for all 49 cases. Relapse severity was assessed through participants' retrospective self-reports during the post-treatment interviews by comparing the severity of recurrent acne with that before isotretinoin treatment. Recurrence was classified as less severe, similar or more severe. This subjective, recall-based assessment was not based on a standardized clinician-rated acne severity scale. The main exposure, cumulative dose, was categorized as 121-150 mg/kg or ≤120 mg/kg, with additional dose categories examined. Other variables included age, sex, BMI, marital status, smoking, family history of acne, acne site, diet, treatment-course history, duration, relapse timing and severity and adverse effects. Previous isotretinoin treatment was not an exclusion criterion. The total number of isotretinoin courses included those received before or after the index course up to the time of assessment and was summarized as descriptive treatment history rather than treated as a baseline predictor of relapse. BMI was expressed

in kg/m² and categorized as <18.5, 18.5-24.9 or ≥25 kg/m². Smoking status reflected current smoking; height and weight used for BMI were measured at treatment initiation.

Statistical Analysis

Data were analyzed using SPSS version 25. Categorical variables were summarized as frequencies and percentages; continuous variables were summarized as mean±standard deviation, when appropriate. Pearson's chi-square or exact tests were used for categorical comparisons as appropriate. For Tables 5-7, Fisher's exact test was used for smoking status, dry lips and elevated liver enzymes; Pearson's chi-square test was used for the other comparisons, except for the age-group comparison (Fisher-Freeman-Halton exact test). A p-value <0.05 was considered statistically significant. Numerical trends and category-specific percentages were interpreted descriptively; multiple exploratory and sparse-subgroup comparisons warranted caution. No multivariable modeling or adjustment for potential confounders was performed; therefore, the reported associations should be interpreted as unadjusted. Given the modest analytic sample (n = 116), these comparisons were exploratory rather than confirmatory. Missing or incomplete medical-record information was supplemented by participant interviews when available. Because the retrospective dataset did not consistently contain detailed information on adherence, baseline acne severity, hormonal factors or maintenance therapy, these variables could not be comprehensively assessed. After supplementing medical-record information with participant interviews, no missing values remained for the variables included in the reported analyses. Clinical variables that were not consistently collected were excluded from the corresponding analyses. Table denominators reflected the relevant study population or subgroup and did not vary because of missing data.

Ethical Considerations

Ethical approval was obtained from the Scientific Research and Ethics Committee, Faculty of Medicine, Al-Baha University (REC/MED/BU-FM/2023/20) and the Research Ethics Committee of Prince Mishari Bin Saud Hospital, Ministry of Health, Al-Baha, Saudi Arabia. The study was conducted in accordance with the Declaration of Helsinki and relevant institutional requirements. All data were de-identified before analysis, stored securely and accessed only by authorized members of the research team. No identifying information was included in the study database or manuscript. Verbal informed consent was obtained from all participants before the post-treatment interview.

RESULTS

Participant Characteristics

A total of 205 patients with acne vulgaris who received oral isotretinoin therapy were initially assessed. Of these, 89 patients did not complete the prescribed treatment course and were excluded. Among the excluded patients, 50 discontinued treatment without a specified reason, 19 because of drug unavailability, 13 because of drug-related adverse effects, 4 because of acne improvement before treatment completion and 3 for other reasons. The final analysis therefore included 116 treatment completers (Table 1). All 116 treatment completers participated in the post-treatment interviews, with no refusals or nonrespondents. The excluded group represented 43.4% of all initially assessed patients (89/205); therefore, the relapse analysis reflects treatment completers rather than all patients initially assessed or prescribed oral isotretinoin. Participant flow is summarized in Figure 1.

Participant sociodemographic characteristics are summarized in Table 2. Most participants were female (83/116, 71.6%), whereas 33 (28.4%) were male. The mean age was 23±4.3 years. The largest age group was 21-30 years (83/116, 71.6%), followed by participants aged 18-20 years (27/116, 23.3%) and those aged 31-40 years (6/116, 5.2%). The mean BMI was 22.7±5.6 kg/m² and the normal-weight BMI category was the most common (72/116, 62.1%). Most participants were single and nonsmokers and most reported a family history of acne.

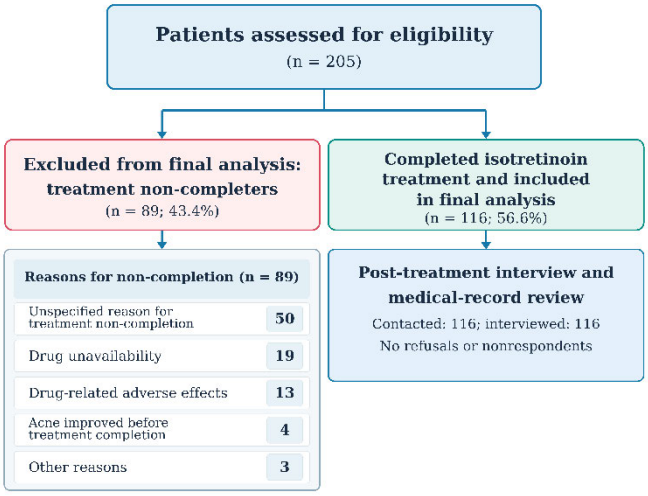


Figure 1: Participant Flow Diagram of the Study Cohort

Table 1: Reasons for Treatment Non-Completion Among Excluded Patients (n = 89)

Reason	n
Unspecified reason for treatment non-completion	50
Drug unavailability	19
Drug-related adverse effects	13
Acne improved before treatment completion	4
Other reasons	3
Total	89

Table 2: Sociodemographic Characteristics of the Patients (n = 116)

Characteristics	n (%)
Sex	
Male	33 (28.4)
Female	83 (71.6)
Age (years)	
Mean±SD	23±4.3
18-20	27 (23.3)
21-30	83 (71.6)
31-40	6 (5.2)
Weight (kg, mean±SD)	59.8±15.2
Height (cm, mean±SD)	162±8.6
BMI (kg/m²)	
Mean±SD	22.7±5.6
<18.5	16 (13.8)
18.5-24.9	72 (62.1)
≥25	28 (24.1)
Marital status	
Single	104 (89.7)
Married	12 (10.3)
Smoking status	
Smoker	10 (8.6)
Nonsmoker	106 (91.4)
Family history of acne	
Yes	83 (71.6)
No	33 (28.4)

BMI: Body mass index, SD: Standard deviation

Acne Characteristics, Treatment Details and Adverse Effects

Table 3 summarizes acne characteristics, treatment details and adverse effects. Facial acne was reported by 109 patients (94.0%) and consumption of milk, high-fat meals or chocolate was reported by 103 patients (88.8%). At the time of assessment, most patients had received one course of isotretinoin (90/116, 77.6%). A total of 30 patients (25.9%) received a cumulative dose of 121-150 mg/kg, whereas 86 (74.1%) received ≤120 mg/kg. The most frequently reported cumulative-dose category was ≤70 mg/kg (39/116, 33.6%), followed by 121-150 mg/kg (30/116, 25.9%), 71-100 mg/kg (27/116, 23.3%) and 101-120 mg/kg (20/116, 17.2%). Cumulative-dose data were complete for all 116 participants, with the entire observed dose distribution represented by the four reported categories (≤70, 71-100, 101-120 and 121-150 mg/kg). Most patients were treated for 6-9 months (91/116, 78.4%).

Adverse effects were common during therapy, as shown in Table 3. Dry lips were reported by 107 patients (92.2%), followed by dry skin in 97 (83.6%) and dry eyes in 88 (75.9%). Additional reported adverse effects included hair loss (68 patients, 58.6%), joint pain (41.4%), depression-like symptoms (37.1%), headache (31.9%), itching (17.2%) and elevated liver enzymes (8.6%). Mucocutaneous symptoms predominated among reported adverse effects. Adverse-effect categories were not mutually exclusive; individual patients could report more than one adverse effect.

Adverse effects were documented in medical records, supplemented by patient interviews when records were incomplete.

Relapse Outcomes

Relapse outcomes are shown in Table 4. During the variable post-treatment follow-up period of 6-18 months, relapse was reported by 49 of 116 treatment completers (42.2%), whereas 67 (57.8%) did not report relapse. This represents a crude observed relapse proportion rather than a fixed-time cumulative incidence estimate. Although the follow-up range was documented, individual follow-up durations could not be recovered to calculate a more detailed follow-up distribution. Among patients who relapsed, recurrence was less severe than baseline in 36 (73.5%), similar in 9 (18.4%) and more severe in 4 (8.2%). Although relapse affected more than two-fifths of treatment completers, most recurrences were milder than the initial presentation. Regarding relapse timing, 11 patients (22.4%) relapsed in less than 6 months, 21 (42.9%) within 6-12 months and 17 (34.7%) after more than 12 months. Overall, 32 of 49 relapses (65.3%) occurred within the first year. Because post-treatment follow-up extended up to 18 months after isotretinoin completion, relapses occurring beyond 12 months were also captured.

Table 3: Acne Characteristics, Habits, Isotretinoin Regimen and Adverse Effects (n = 116)

Variable	n (%)
Localization of acne	
Face	109 (94.0)
Other sites	7 (6.0)
Milk, high-fat meals or chocolate in diet	
Yes	103 (88.8)
No	13 (11.2)
Total number of isotretinoin courses by assessment	
One	90 (77.6)
Two	18 (15.5)
Three	8 (6.9)
Cumulative dose of 121-150 mg/kg	
Yes	30 (25.9)
No	86 (74.1)
Treatment duration (months)	
Less than 6	9 (7.8)
6-9	91 (78.4)
More than 9	16 (13.8)
Cumulative dose (mg/kg)	
≤70	39 (33.6)
71-100	27 (23.3)
101-120	20 (17.2)
121-150	30 (25.9)
Adverse effects	
Dry lips	107 (92.2)
Dry skin	97 (83.6)
Dry eyes	88 (75.9)
Hair loss	68 (58.6)
Joint pain	48 (41.4)
Depression-like symptoms	43 (37.1)
Headache	37 (31.9)
Itching	20 (17.2)
Elevated liver enzymes	10 (8.6)

Table 4: Acne Relapse Among the Patients (n = 116)

Variable	n (%)
Acne relapse	
Yes	49 (42.2)
No	67 (57.8)
Severity of relapse (n = 49)	
Same as before treatment	9 (18.4)
More severe than before treatment	4 (8.2)
Less severe than before treatment	36 (73.5)
Time of relapse (n = 49)	
Less than 6 months	11 (22.4)
6-12 months	21 (42.9)
More than 12 months	17 (34.7)

Sociodemographic Characteristics According to Relapse Status

All comparisons by relapse status in Tables 5-7 were unadjusted and exploratory. Table 5 summarizes sociodemographic characteristics by relapse status. Relapse occurred in 41 of 83 females (49.4%) and 8 of 33 males (24.2%), indicating that the relapse proportion in females was approximately twice that in males. Most patients with relapse were aged 21-30 years and were single. The unadjusted ratio of observed relapse proportions (female versus male) was 2.04 (95% CI, 1.07-3.87).

Risk Factors According to Relapse Status

Table 6 summarizes selected risk factors. Among patients with relapse, 29 (59.2%) had a normal BMI, 12 (24.5%) had a BMI ≥25 kg/m² and 8 (16.3%) had a BMI <18.5 kg/m². Most were nonsmokers (47/49, 95.9%). A positive family history was reported in 37 patients with relapse (75.5%).

Using category-specific denominators, relapse occurred in 7 of 27 patients aged 18-20 years (25.9%), 39 of 83 patients aged 21-30 years (47.0%) and 3 of 6 patients aged 31-40 years (50.0%), although the oldest age group included only six participants. Relapse occurred in 8 of 16 patients with a BMI <18.5 kg/m² (50.0%), 29 of 72 patients with a BMI of 18.5-24.9 kg/m² (40.3%) and 12 of 28 patients with a BMI ≥25 kg/m² (42.9%). Relapse was reported in 2 of 10 smokers (20.0%) and 47 of 106 nonsmokers (44.3%); however, the smoker subgroup was small. This estimate is unstable and unsuitable for clinical inference. Relapse was also reported in 37 of 83 patients with a family history of acne (44.6%) and 12 of 33 patients without a family history (36.4%).

Table 5: Sociodemographic Characteristics According to Relapse Status

Variable	Relapse (n = 49)	Non-relapse (n = 67)	p-value
Sex			
Male	8 (16.3)	25 (37.3)	0.013
Female	41 (83.7)	42 (62.7)	
Age group (years)			
18-20	7 (14.3)	20 (29.9)	0.162
21-30	39 (79.6)	44 (65.7)	
31-40	3 (6.1)	3 (4.5)	
Marital status			
Single	44 (89.8)	60 (89.6)	0.966
Married	5 (10.2)	7 (10.4)	

Values are presented as n (%), Percentages are calculated within the relapse and non-relapse groups and are presented as column percentages. By contrast, sex-specific relapse proportions reported in the text use the total number of patients of each sex as the denominator

Table 6: Risk Factors According to Relapse Status

Variable	Relapse (n = 49)	Non-relapse (n = 67)	p-value
BMI (kg/m²)			
<18.5	8 (16.3)	8 (11.9)	0.774
18.5-24.9	29 (59.2)	43 (64.2)	
≥25	12 (24.5)	16 (23.9)	
Smoking status			
Smoker	2 (4.1)	8 (11.9)	0.187
Nonsmoker	47 (95.9)	59 (88.1)	
Family history of acne			
Yes	37 (75.5)	46 (68.7)	0.419
No	12 (24.5)	21 (31.3)	

BMI: Body mass index. Values are presented as n (%). Percentages are calculated within the relapse and non-relapse groups and are presented as column percentages

Table 7: Treatment Details and Adverse Effects According to Relapse Status (n = 116)

Variable	Relapse (n = 49)	Non-relapse (n = 67)	p-value
Received 121-150 mg/kg as a cumulative dose			
Yes	11 (22.4)	19 (28.4)	0.473
No	38 (77.6)	48 (71.6)	
Cumulative dose (mg/kg)			
≤70	18 (36.7)	21 (31.3)	0.868
71-100	12 (24.5)	15 (22.4)	
101-120	8 (16.3)	12 (17.9)	
121-150	11 (22.4)	19 (28.4)	
Adverse effects			
Dry lips	44 (89.8)	63 (94.0)	0.490
Dry skin	41 (83.7)	56 (83.6)	0.990
Dry eyes	38 (77.6)	50 (74.6)	0.716
Itching	8 (16.3)	12 (17.9)	0.823
Hair loss	33 (67.3)	35 (52.2)	0.103
Elevated liver enzymes	4 (8.2)	6 (9.0)	1.000
Joint pain	26 (53.1)	22 (32.8)	0.029
Headache	17 (34.7)	20 (29.9)	0.580
Depression-like symptoms	16 (32.7)	27 (40.3)	0.400

Values are presented as n (%). Percentages are calculated within the relapse and non-relapse groups and are presented as column percentages. Category-specific relapse rates were calculated within each cumulative-dose category: ≤70 mg/kg, 18/39 (46.2%); 71-100 mg/kg, 12/27 (44.4%); 101-120 mg/kg, 8/20 (40.0%) and 121-150 mg/kg, 11/30 (36.7%). The binary comparison was included to examine the higher cumulative-dose group in relation to the conventional treatment target

Treatment-Related Factors and Adverse Effects According to Relapse Status

Table 7 presents treatment-related factors and adverse effects by relapse status. Category-specific relapse rates were highest in the ≤70 mg/kg group (18/39, 46.2%), followed by the 71-100 mg/kg group (12/27, 44.4%), the 101-120 mg/kg group (8/20, 40.0%) and the 121-150 mg/kg group (11/30, 36.7%). The lowest observed relapse proportion was in the 121-150 mg/kg group. Joint pain during isotretinoin treatment was more frequent among patients with relapse than among those without relapse (53.1% versus 32.8%), whereas dry lips, dry skin and dry eyes were common in both groups. These findings show a numerical decrease in relapse rates across increasing cumulative-dose categories, although no statistically significant association was observed. With 121-150 mg/kg as the reference, the unadjusted ratios of observed relapse proportions (95% CIs) were 1.26 (0.70-2.25) for ≤70 mg/kg, 1.21 (0.64-2.28) for 71-100 mg/kg and 1.09 (0.53-2.23) for 101-120 mg/kg.

DISCUSSION

This study assessed acne relapse after oral isotretinoin therapy among treatment completers at Prince Mishari Bin

Saud Hospital in Al-Baha Province. Relapse was reported in 49 of 116 patients (42.2%), indicating that relapse remains a common post-treatment issue. Relapse severity, however, provides important clinical context. Among patients who relapsed, 36 of 49 (73.5%) described recurrence as milder than baseline, corresponding to 36 of 116 treatment completers (31.0%), whereas only 4 (8.2%) reported more severe recurrence. Across the full cohort, only 13 of 116 patients (11.2%) experienced relapse that was similar to or worse than baseline and only 4 patients (3.4%) had more severe recurrence. Thus, although relapse was frequent, most patients retained meaningful improvement after isotretinoin therapy.

The relapse proportion observed in this study is comparable to that reported by Alshammari et al., who reported relapse in 45.12% of patients treated with isotretinoin [18]. It is also higher than the approximately 36% relapse rate reported in a Sudanese cohort [19]. Between-study variation may reflect differences in relapse definitions, follow-up duration, baseline acne severity, dosing regimens, adherence, use of maintenance therapy, hormonal factors and population characteristics. A Colombian study also suggested that maintenance therapy after isotretinoin may reduce the likelihood of relapse [20]. Together, these findings suggest that treatment exposure and post-treatment management may both contribute to recurrence.

Previous studies have examined treatment-related factors potentially associated with relapse. Azoulay *et al.* [21] reported an association between relapse and treatment exposure, whereas Blasiak *et al.* [22] reported lower relapse and retreatment rates after high-dose isotretinoin, although higher doses may raise tolerability concerns. More recently, Lai and Barbieri [23] identified relapse and isotretinoin retreatment as important post-treatment outcomes. In the present cohort, the relapse rate showed a numerical decline across cumulative-dose categories: 46.2% in the ≤70 mg/kg group, 44.4% in the 71-100 mg/kg group, 40.0% in the 101-120 mg/kg group and 36.7% in the 121-150 mg/kg group. This pattern reflects lower observed relapse proportions in groups with higher cumulative exposure.

The observed cumulative-dose pattern warrants cautious interpretation. The retrospective design, unequal group sizes and incomplete adherence and maintenance-therapy data limit causal inference. Baseline acne severity, clinician dosing decisions, treatment duration, adherence, treatment-end clearance and tolerability may have confounded the observed dose-relapse pattern. Rademaker [24] emphasized that isotretinoin outcomes should be considered in relation to dose, duration, clearance, tolerability and ongoing disease activity rather than cumulative dose alone. The same author later questioned rigid cumulative-dose thresholds and supported a more individualized approach [25]. Tran *et al.* [26] also showed that patients requiring a second course of isotretinoin may have distinct clinical characteristics. Accordingly, the dose-related trend should be viewed as a descriptive finding rather than evidence of causality.

Despite its high efficacy, isotretinoin does not eliminate the possibility of relapse. Zouboulis [27] noted that recurrence may be influenced by sex, age, severity, seborrhea, hormonal factors and treatment-related characteristics. Liu *et al.* [28] also reported recurrence after isotretinoin therapy and long-term follow-up data indicate that acne may recur years after treatment completion [29]. These findings support balanced patient counseling: although isotretinoin is highly effective, permanent remission cannot be guaranteed.

Relapse timing also has clinical implications. In this study, 32 of 49 relapses (65.3%) occurred within the first 12 months after treatment completion. This finding supports the value of structured follow-up during the first year, when early recurrence can be identified and managed with topical maintenance therapy, hormonal evaluation when appropriate or additional treatment.

Female patients had a higher observed relapse proportion than male patients (49.4% versus 24.2%). This comparison warrants caution because female patients constituted most of the cohort. Nevertheless, the pattern is clinically plausible. Adult female acne, hormonal fluctuations, cosmetic concerns and healthcare-seeking behavior may contribute to persistence, recurrence or increased recognition of relapse. These remain hypotheses for future research rather than findings of this cohort. Relapse may also affect quality of life and productivity [30] and adult acne differs from adolescent acne in several sex-related patterns [31]. Future studies should assess menstrual irregularities, polycystic ovary syndrome, oral contraceptive use, anti-androgen therapy, the distribution of adult female acne and maintenance treatment.

A family history of acne was common among patients who relapsed, with 37 of 49 relapsed patients (75.5%) reporting a positive family history. Genetic predisposition may influence acne onset and clinical phenotype, as described by Šijak *et al.* [32]. However, because family history was also common in the overall cohort, this finding is descriptive and does not establish predictive value.

No clear association between BMI and relapse was observed in this cohort. Most patients who relapsed were in the normal BMI category, which reflected the distribution of the overall sample. Although previous research has suggested an association between higher BMI and acne severity in adolescents [33], the present findings do not allow firm conclusions regarding BMI as a predictor of relapse.

Adverse effects were common, particularly dry lips, dry skin and dry eyes. Joint pain was reported more frequently among patients with relapse than among those without relapse, but this difference may be influenced by recall bias, activity level, cumulative exposure or individual variability in symptom reporting. Because adverse effects may influence adherence and treatment satisfaction, proactive counseling and supportive care are important throughout treatment. Psychological factors may also influence adherence to acne treatment among Saudi patients [34].

Patient education remains a key component of isotretinoin therapy. Saudi data indicate persistent

knowledge gaps among female patients regarding isotretinoin use [35]. Counseling should address expected mucocutaneous dryness, monitoring requirements, teratogenicity and pregnancy prevention when applicable, adherence, the risk of relapse and post-treatment follow-up.

Several limitations should be considered when interpreting these findings. The retrospective design precludes causal inference. Some relapse-related data were based on patient recall and supplemented by available records. In addition, no multivariable adjustment was performed; therefore, the observed associations may be affected by confounding and should not be interpreted as independent predictors. The analysis was restricted to patients who completed isotretinoin therapy and detailed information on baseline acne severity, adherence, hormonal factors and post-treatment maintenance therapy was not consistently available. Lesion type and scarring status were not evaluated in the reported analyses. The absence of standardized acne severity assessments at baseline and after treatment may have introduced misclassification of improvement, clearance and subsequent relapse. Because post-treatment follow-up varied from 6 to 18 months, participants with shorter follow-up had less opportunity for relapse to be detected. Individual follow-up durations were not recoverable for a time-to-event analysis. Consequently, the observed relapse proportion should not be interpreted as cumulative incidence at a standardized follow-up time. Incomplete documentation of some clinical variables may also have introduced information bias. Excluding 89 non-completers (43.4%) may have introduced selection bias if adherence, tolerability or drug access differed, limiting generalizability to all patients prescribed isotretinoin. Despite these limitations, this study provides regional data on relapse frequency, recurrence severity, first-year relapse timing and cumulative-dose patterns after completion of isotretinoin therapy. The principal clinical message is that relapse was common but most recurrences were milder than baseline acne. This distinction may help reduce patient anxiety and support continued engagement with dermatology care. Patients with lower cumulative exposure, female patients with possible hormonal influences and those with early recurrence may benefit from closer follow-up—a hypothesis requiring prospective validation. Future studies should also distinguish true inflammatory relapse from mild comedonal recurrence and document the use of topical retinoids or hormonal therapy after treatment completion. Such information may inform relapse-prevention strategies in routine dermatology practice.

CONCLUSIONS

Among treatment completers in Al-Baha Province, acne relapse after oral isotretinoin therapy occurred in 49 of 116 patients (42.2%). Most recurrent episodes were milder than baseline, as reported by 36 of 49 relapsed patients (73.5%). Among patients who relapsed, 32 (65.3%) experienced relapse within the first year. Observed relapse proportions were higher among female than male patients (49.4% versus 24.2%). A numerical decline in relapse rates was observed across increasing cumulative-dose categories, from 46.2% in the ≤70 mg/kg group to 36.7% in the 121-150 mg/kg group. Clinical considerations include individualized dosing, proactive adverse-effect management, maintenance therapy when appropriate, patient education and structured follow-up, particularly during the first post-treatment year. Larger prospective studies are needed to evaluate potential predictors of relapse using standardized definitions, severity grading, adherence assessment, hormonal evaluation, maintenance therapy data and longer follow-up across a broader range of regional practice settings.

Acknowledgement

The authors thank the Dermatology Department at Prince Mishari Bin Saud Hospital and all participants for their support.

Ethical Statement

Ethical approval was obtained from the Scientific Research and Ethics Committee, Faculty of Medicine, Al-Baha University (REC/MED/BU-FM/2023/20) and the Research Ethics Committee of Prince Mishari Bin Saud Hospital, Ministry of Health, Al-Baha, Saudi Arabia. The study was conducted in accordance with the Declaration of Helsinki and relevant institutional requirements.

REFERENCES

[1] Heng, A.H.S. and F.T. Chew. "Systematic Review of the Epidemiology of Acne Vulgaris." *Scientific Reports*, vol. 10, no. 1, 2020. https://doi.org/10.1038/s41598-020-62715-3.

[2] Tan, J.K.L. and K. Bhate. "A Global Perspective on the Epidemiology of Acne." *British Journal of Dermatology*, vol. 172, no. S1, 2015, pp. 3-12. https://doi.org/10.1111/bjd.13462.

[3] Alsohaimi, A.O. *et al.* "Prevalence of Acne Vulgaris in Adolescents and Young Adults in Al-Baha Region, Saudi Arabia." *Cureus*, vol. 16, no. 10, 2024. https://doi.org/10.7759/cureus.71293.

[4] Alanazi, T.M. *et al.* "Prevalence of Acne Vulgaris, Its Contributing Factors and Treatment Satisfaction among the Saudi Population in Riyadh, Saudi Arabia: A Cross-Sectional Study." *Journal of Dermatology and Dermatologic Surgery*, vol. 24, no. 1, 2020, pp. 33-37. https://doi.org/10.4103/jdds.jdds_71_19.

[5] Allayali, A.Z. *et al.* "Assessment of Prevalence, Knowledge, Attitude and Psychosocial Impact of Acne Vulgaris among Medical Students in Saudi Arabia." *Journal of Clinical and Experimental Dermatology Research*, vol. 8, no. 4, 2017. https://doi.org/10.4172/2155-9554.1000404.

[6] Deyab, A.A. *et al.* "Prevalence, Awareness and Psychological Impact of Acne Vulgaris among University Students." *Journal of Research in Medical and Dental Science*, vol. 8, no. 1, 2020, pp. 68-73. https://www.jrmds.in/articles/prevalence-awareness-and-psychological-impact-of-acne-vulgaris-among-university-students-45470.html.

[7] Alqahtani, A. *et al.* "Psychological Impact of Acne Vulgaris on the Young Saudi Population." *Cureus*, vol. 13, no. 12, 2021. https://doi.org/10.7759/cureus.20509.

[8] Zaenglein, A.L. *et al.* "Guidelines of Care for the Management of Acne Vulgaris." *Journal of the American Academy of Dermatology*, vol. 74, no. 5, 2016, pp. 945-973.e33. https://doi.org/10.1016/j.jaad.2015.12.037.

[9] Reynolds, R.V. *et al.* "Guidelines of Care for the Management of Acne Vulgaris." *Journal of the American Academy of Dermatology*, vol. 90, no. 5, 2024, pp. 1006.e1-1006.e30. https://doi.org/10.1016/j.jaad.2023.12.017.

[10] Kraft, J. and A. Freiman. "Management of Acne." *Canadian Medical Association Journal*, vol. 183, no. 7, 2011, pp. E430-E435. https://doi.org/10.1503/cmaj.090374.

[11] Layton, A. "The Use of Isotretinoin in Acne." *Dermato-Endocrinology*, vol. 1, no. 3, 2009, pp. 162-169. https://doi.org/10.4161/derm.1.3.9364.

[12] Bettoli, V. *et al.* "Challenges and Solutions in Oral Isotretinoin in Acne: Reflections on 35 Years of Experience." *Clinical, Cosmetic and Investigational Dermatology*, vol. 12, 2019, pp. 943-951. https://doi.org/10.2147/CCID.S234231.

[13] Daly, A.U. *et al.* "A Systematic Review of Isotretinoin Dosing in Acne Vulgaris." *JEADV Clinical Practice*, vol. 2, no. 3, 2023, pp. 432-449. https://doi.org/10.1002/jvc2.154.

[14] Vallerand, I.A. *et al.* "Efficacy and Adverse Events of Oral Isotretinoin for Acne: A Systematic Review." *British Journal of Dermatology*, vol. 178, no. 1, 2018, pp. 76-85. https://doi.org/10.1111/bjd.15668.

[15] Lee, Y.H. *et al.* "Laboratory Monitoring during Isotretinoin Therapy for Acne: A Systematic Review and Meta-Analysis." *JAMA Dermatology*, vol. 152, no. 1, 2016, pp. 35-44. https://doi.org/10.1001/jamadermatol.2015.3091.

[16] Alghamdi, W.A. *et al.* "Knowledge, Attitude and Practice Regarding the Use of Isotretinoin in Saudi Arabia." *Cureus*, vol. 15, no. 12, 2023. https://doi.org/10.7759/cureus.50516.

[17] Alshaalan, Z.M. "Knowledge on the Use of Isotretinoin and Its Side Effects and Awareness towards Saudi FDA-Pregnancy Prevention Program among the Female Acne Patients: A Northern Saudi Study." *Medicina*, vol. 58, no. 11, 2022. https://doi.org/10.3390/medicina58111609.

[18] Alshammari, S.A. *et al.* "Prevalence and Associated Risk Factors of Acne Relapse among Saudi Acne Vulgaris Patients Using Isotretinoin." *Saudi Pharmaceutical Journal*, vol. 28, no. 3, 2020, pp. 374-379. https://doi.org/10.1016/j.jsps.2020.01.019.

[19] Ibrahim, S. *et al.* "Acne Vulgaris Relapse in Sudanese Patients Treated with Oral Isotretinoin: Rate and Predictive Factors." *Journal of Multidisciplinary Healthcare*, vol. 16, 2023, pp. 839-849. https://doi.org/10.2147/JMDH.S405509.

[20] Morales-Cardona, C.A. and G. Sánchez-Vanegas. "Acne Relapse Rate and Predictors of Relapse Following Treatment with Oral Isotretinoin." *Actas Dermo-Sifiliográficas*, vol. 104, no. 1, 2013, pp. 61-66. https://doi.org/10.1016/j.ad.2012.05.004.

[21] Azoulay, L. *et al.* "Isotretinoin Therapy and the Incidence of Acne Relapse: A Nested Case-Control Study." *British Journal of Dermatology*, vol. 157, no. 6, 2007, pp. 1240-1248. https://doi.org/10.1111/j.1365-2133.2007.08250.x.

[22] Blasiak, R.C. *et al.* "High-Dose Isotretinoin Treatment and the Rate of Retrial, Relapse and Adverse Effects in Patients with Acne Vulgaris." *JAMA Dermatology*, vol. 149, no. 12, 2013, pp. 1392-1398. https://doi.org/10.1001/jamadermatol.2013.6746.

[23] Lai, J. and J.S. Barbieri. "Acne Relapse and Isotretinoin Retrial in Patients with Acne." *JAMA Dermatology*, vol. 161, no. 4, 2025, pp. 367-374. https://doi.org/10.1001/jamadermatol.2024.5416.

[24] Rademaker, M. "Isotretinoin: Dose, Duration and Relapse. What Does 30 Years of Usage Tell Us?" *Australasian Journal of Dermatology*, vol. 54, no. 3, 2013, pp. 157-162. https://doi.org/10.1111/j.1440-0960.2012.00947.x.

[25] Rademaker, M. "Making Sense of the Effects of the Cumulative Dose of Isotretinoin in Acne Vulgaris." *International Journal of Dermatology*, vol. 55, no. 5, 2016, pp. 518-523. https://doi.org/10.1111/ijd.12942.

[26] Tran, P.T. *et al.* "Analysis of Factors Associated with Relapse in Patients on Their Second Course of Isotretinoin for Acne Vulgaris." *Journal of the American Academy of Dermatology*, vol. 84, no. 3, 2021, pp. 856-859. https://doi.org/10.1016/j.jaad.2020.10.030.

[27] Zouboulis, C.C. "The Truth behind This Undeniable Efficacy—Recurrence Rates and Relapse Risk Factors of Acne Treatment with Oral Isotretinoin." *Dermatology*, vol. 212, no. 2, 2006, pp. 99-100. https://doi.org/10.1159/000090646.

[28] Liu, A. *et al.* "Relapse of Acne Following Isotretinoin Treatment: A Retrospective Study of 405 Patients." *Journal of Drugs in Dermatology*, vol. 7, no. 10, 2008, pp. 963-966. https://pubmed.ncbi.nlm.nih.gov/19112761/.

[29] Nascimento, C.R. *et al.* "Acne Recurrence after Treatment with Oral Isotretinoin: 5-Year Follow-Up." *Surgical and Cosmetic Dermatology*, vol. 3, no. 3, 2011, pp. 188-191. https://www.redalyc.org/articulo.oa?id=265522087008.

[30] Dréno, B. *et al.* "Acne Relapses: Impact on Quality of Life and Productivity." *Journal of the European Academy of Dermatology and Venereology*, vol. 33, no. 5, 2019, pp. 937-943. https://doi.org/10.1111/jdv.15419.

[31] Skroza, N. *et al.* "Adult Acne versus Adolescent Acne: A Retrospective Study of 1,167 Patients." *The Journal of Clinical and Aesthetic Dermatology*, vol. 11, no. 1, 2018, pp. 21-25. https://pmc.ncbi.nlm.nih.gov/articles/PMC5788264/.

[32] Šijak, D. *et al.* "Correlation between Family History and the Age of Onset of Childhood Acne in Relation to Sex and Type of Acne." *Acta Dermatovenerologica Croatica*, vol. 27, no. 2, 2019, pp. 86-89. https://hrcak.srce.hr/223231.

[33] Sas, K. and A. Reich. "High Body Mass Index Is a Risk Factor for Acne Severity in Adolescents: A Preliminary Report." *Acta Dermatovenerologica Croatica*, vol. 27, no. 2, 2019, pp. 81-85. https://hrcak.srce.hr/223230.

[34] Alghofaili, A. *et al.* "The Effect of Depression on Treatment Adherence among a Sample of Saudi Patients Diagnosed with Acne Vulgaris." *Clinical, Cosmetic and Investigational Dermatology*, vol. 14, 2021, pp. 1497-1506. https://doi.org/10.2147/CCID.S335007.

[35] Bakheet, K.M.A. *et al.* "Females' Knowledge and Use of Isotretinoin (Roaccutane) in the Western Region of Saudi Arabia." *Cureus*, vol. 12, no. 12, 2020. https://doi.org/10.7759/cureus.12148.