folia medica

Folia Medica 68(5)
DOI: 10.3897/folmed.68.e185886

Research Article

Monitoring adverse drug reactions of isotretinoin: a prospective observational study

Qutaiba A. Qasim[1], Jubran K. Hassan[2], Kadhim Ali Kadhim[3], Hany Akeel Al-hussaniy[4,5]

1 *Department of Clinical Laboratory Sciences, College of Pharmacy, University of Basrah, Basrah, Iraq*
2 *Department of Clinical Pharmacy, College of Pharmacy, University of Basrah, Basrah, Iraq*
3 *College of Medicine, University of Baghdad, Baghdad, Iraq*
4 *Department of Pharmacology, College of Pharmacy, Al-Nisour University, Baghdad, Iraq*
5 *Dr Hany Akeel Institute, Iraqi Medical Research Center, Baghdad, Iraq*

Corresponding author: Qutaiba Qasim, Department of Clinical Laboratory Sciences, College of Pharmacy, University of Basrah, Basrah, Iraq; Email: qutaibaqasim71@gmail.com

Received: 21 January 2026 ♦ **Accepted:** 25 March 2026 ♦ **Published:** 30 October 2026

Citation: Qasim QA, Hassan JK, Kadhim KA, Al-hussaniy HA. Monitoring adverse drug reactions of isotretinoin: a prospective observational study. Folia Med (Plovdiv) 2026;68(5):e185886. doi: 10.3897/folmed.68.e185886.

Abstract

Introduction: Acne vulgaris is very common and may have a significant psychosocial effect. Moderate to severe acne is best treated using oral isotretinoin, which has a wide spectrum of adverse drug reactions (ADRs).

Aim: To characterize the occurrence, pattern, and severity of isotretinoin-related ADRs in the Iraqi dermatology clinics and clarify clinical and treatment factors linked to its frequency.

Patients and methods: This was a prospective observational cohort study carried out at two of the outpatient dermatology clinics in Basra city between January 2024 and December 2025. Patients were recruited consecutively as they were aged 12 years and older and had been taking systemic isotretinoin as the main form of therapy against acne.

Results: Out of 420 patients who were screened, 400 patients qualified. The mean age was 21.8 years, and the SD was 4.7 years; 55% of the population was female, and 90% had moderate or severe acne. In general, 360 patients (90%) had at least one ADR, which led to 965 events. The most common were mucocutaneous reactions (88.5% of patients); then there were laboratory abnormalities (22%) and musculoskeletal complaints (around 15%-16%). Biochemical abnormalities were generally mild to moderate, while clinically significant psychiatric events were rare. Moderate/severe ADRs were independently related to female sex, baseline dyslipidemia, and daily dose ≥0.5 mg/kg/day.

Conclusion: With the aid of organized monitoring, risk-specific dosing, and strong pregnancy prevention and counseling measures, isotretinoin may be deployed effectively and in a relatively safe way in the Iraqi dermatology clinics.

Keywords

acne vulgaris, dermatology, isotretinoin, prospective studies

Introduction

Acne vulgaris is one of the most common skin diseases in the world; it is a long-lasting inflammation of the pilosebaceous unit. It is commonly marked by comedones, papules, pustules, and nodules and, in some cases, permanent scarring, particularly on the face, chest, and back.[1] According to population-based studies and estimates of Global Burden of Disease, acne, according to the sources, has a significant proportion of adolescents and youthful adults,

Copyright by authors. This is an open access article distributed under the terms of the Creative Commons Attribution License (CC-BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

and lifetime occurrence of acne is up to 80-90 percent in cohorts, and there is an impressive number of cases into adulthood. Recent studies have highlighted its high psychosocial and quality-of-life (QoL) effect. The patients usually report levels of embarrassment, social withdrawal, and reduced self-esteem, including education and career issues. Lashti and colleagues conducted a recent review of the system and found that there is a constant impact of negative effects on health-related quality of life (HRQoL) in acne on emotional, social, functional, and similar scales compared to other long-term health conditions.[2] The fact that there is substantial research on observational studies confirms the hypothesis that a larger score in clinical severity is associated with poorer HRQoL and more distress.[3,4]

Acne has also been identified to cause mental health outcomes, including depression and anxiety, symptoms, and suicidal ideation. The existing clinical practice recommendations focus on the active acknowledgment of the psychological outcomes of the acne by clinicians, as the emergence of visible lesions on the face and other exposed areas can result in stigma, bullying, and body image disruption.[5] When acne is poorly managed, it may cause permanent scars and post-inflammatory dyspigmentation, and this may continue to propagate psychosocial impairment even after the active inflammation has healed.[6,7]

Even though isotretinoin has been widely used clinically for several decades, and the key adverse effects are well known, there are still significant gaps in understanding how reactions are measured and managed in the daily dermatology clinic. In large parts, the safety data is obtained from clinical trials or highly selected cohorts that adhere to stringent inclusion criteria and a schedule-based protocol in the laboratory.[6] These circumstances are unlikely to be realistic in practice, where patients will vary in their adherence, present with a range of comorbidities, and have variable access to follow-up.[8] The current pharmacovigilance studies and regulatory evaluations have indicated that the issues persist, especially when it comes to pregnancy prevention, wherein, in certain countries, even with well-established PPPs, isotretinoin-exposed pregnancies are still reported.[9]

Meanwhile, a shift in prescribing is also taking place, with low-dose regimens, treatment of wider age groups, and the delivery of isotretinoin in non-hospital and home-based dermatology on the increase.[10] The number of current, clinic-based, observational studies that thoroughly outline the frequency, pattern, and severity of isotretinoin-related adverse responses and assess the extent to which recommended monitoring guidelines, including routine laboratory examinations, counseling documentation, and pregnancy counselling measures, are adhered to in practice is less than one might expect.[11] These lapses become particularly glaring in low- and medium-income regions as well as in health systems with immature pharmacovigilance. Standardized and higher-quality data on daily dermatology cases are therefore needed to influence local practice guidelines, develop surveillance mechanisms, and assume a more secure method of using isotretinoin.[12]

Acne vulgaris is a widespread chronic condition having serious physical and psychosocial consequences. Another important treatment regimen that the patients with moderate-to-severe disease or treatment-resistant disease should consider is systemic isotretinoin. Long-term remission is possible, and scarring can be eliminated.[13] Nevertheless, isotretinoin is linked to a complicated range of adverse drug events, such as ubiquitous mucocutaneous alteration, which may be severe laboratory anomalies, severe teratogenicity, and musculoskeletal and potentially neuropsychiatric reactions.[14,15] Laboratory surveillance, pregnancy prevention, and clinical follow-up have been given comprehensive recommendations by the regulatory bodies and professional societies.[16] Nevertheless, the evidence presented shows that these guidelines are not always adhered to in the everyday practice of dermatology, and isotretinoin-exposed pregnancies and other avoidable and unwanted results still happen.[17]

Aim

The current study aimed to assess the frequency and pattern of adverse drug reactions associated with isotretinoin therapy in dermatology clinics; evaluate the severity of isotretinoin-related adverse drug reactions using standardized assessment criteria; identify patient- and treatment-related risk factors for adverse drug reactions, including age, sex, comorbidities, concomitant drugs, daily dose, and cumulative dose; and assess adherence to recommended clinical and laboratory monitoring during isotretinoin therapy in participating dermatology clinics, including baseline and follow-up investigations, documentation of patient counseling, and pregnancy prevention measures where applicable.

Patients and methods

Study design and setting

The study was a prospective observational cohort conducted in outpatient dermatology clinics in Basra. The primary purpose was to observe and describe adverse drug reactions (ADRs) in patients treated with systemic isotretinoin for acne.[18] Two outpatient dermatology clinics in Basra, Iraq, conducted the study. These clinics are referral centers for moderate-to-severe acne from primary and secondary health facilities and also offer specialized acne treatment, including isotretinoin. The research period was from January 2024 to December 2025, enabling the incorporation of new courses on isotretinoin into the study and allowing 6 months as the minimum follow-up period for most participants. The data were collected in clinic visits and, when needed, using structured telephone follow-up.

Inclusion and exclusion criteria

Eligibility screening of all consecutive patients enrolled in the study who presented to the participating dermatology clinics within the study period and were prescribed systemic isotretinoin to treat acne was done based on predefined criteria. The study also required the participants to have a clinical diagnosis of acne vulgaris that warrants systemic isotretinoin therapy, be age 12 years and above, have either just started on isotretinoin or be receiving treatment at the time of the study, and be willing and able to attend the scheduled follow-up visits. The patients were eliminated when they lacked incomplete or missing baseline clinical or laboratory data; had less than four weeks of isotretinoin therapy; were pregnant or breastfeeding at the time of the baseline; or used isotretinoin to treat something other than acne. The inclusion criteria were extremely liberal, and only patients who met all the requirements of inclusion and none of the exclusion criteria were eligible to participate.

Sampling and sample size

The sampling method employed was a consecutive sampling design, in which all eligible patients were enrolled in the study. A single-proportion formula was used to estimate the target sample size, assuming a 50% prevalence of any ADR (to maximize the sample size in the event of uncertainty), a confidence level of 95%, and an error of 5%. The minimum required sample size was estimated at 384 patients, accounting for a 10% loss to follow-up, and a target of 420 patients was set to achieve the necessary power. During the study period, 420 patients were screened. Twenty patients were excluded due to missing records or not meeting the inclusion criteria, leaving a final cohort of 400 patients.

Data collection procedures

Data were collected using a standardized case report form (CRF) developed for the study. Information was gathered from three primary sources: medical records and clinic files (including electronic health records where available), laboratory reports from private central laboratories, and patient interviews, which were conducted in person during scheduled visits and, if necessary, by phone. For each patient, data were collected at baseline (initiation or first documented visit on isotretinoin) and at follow-up visits typically scheduled every 4-8 weeks, in accordance with routine clinic practice. The grades of adverse drug reactions (ADRs) were rated on Common Terminology Criteria of Adverse Events (CTCAE) version 5.0. The grading of events was done using this standardized system, with mild, moderate, and severe (Grade 1, Grade 2, and Grade 3) events.

Monitoring schedule

Baseline assessment included a clear history and physical examination, assessment of acne severity, and collection of pertinent laboratory tests (liver function tests, fasting lipid profile, and CBC). A negative pregnancy test result in women who had the potential to give birth had to be documented before starting isotretinoin and then periodically during treatment in accordance with local risk reduction measures.[19]

Generally, follow-ups were scheduled after every 4-8 weeks, and the clinicians noted new or persistent ADRs, comorbid medications, dose changes, and adherence. Laboratory tests were repeated every 8-12 weeks, or more often if clinically necessary (e.g., the presence of liver disease or lipid disorders).

Sample size calculation

The sample size was calculated to estimate the prevalence of any ADR among isotretinoin-treated patients with acceptable precision. Assuming an ADR prevalence (p) of 0.50 (conservative estimate to maximize sample size), a 95% confidence level (Z=1.96), and a margin of error (d) of 0.05, the initial sample size (n) was derived from the formula:

$$n = \frac{Z^2\, p(1-p)}{d^2}$$

Substituting the values:

$$n = \frac{(1.96)^2 \times 0.5 \times 0.5}{(0.05)^2} \approx 384$$

To account for an estimated 10% non-response or loss to follow-up, the adjusted sample size was:

$$n_{\text{adjusted}} = \frac{384}{1 - 0.10} \approx 427$$

Given logistical considerations and anticipated patient flow, a target of 420 patients was deemed feasible. Ultimately, 400 patients provided complete baseline and follow-up data suitable for analysis **(Table 1)**.

Table 1. Sample size assumptions and final cohort

Parameter	Value
Assumed prevalence of any ADR (p)	50%
Confidence level	95% (Z=1.96)
Margin of error (d)	5%
Initial calculated sample size	384
Anticipated loss to follow-up	10%
Target sample size	420
Final number of patients analyzed	400

Results

Baseline characteristics

The patients who were screened during the study period were 420, receiving systemic isotretinoin to treat acne.

Folia Medica

Twenty patients were excluded: 12 because they lacked 10 weeks of baseline laboratory data, 5 because their isotretinoin treatment lasted less than 4 weeks, and 3 because isotretinoin was prescribed for non-acne indicators (e.g., rosacea and folliculitis). The analytic cohort that came last had 400 patients **(Fig. 1)**.

Demographic and clinical profile

The mean age of the cohort was 21.8±4.7 years (range 13–36 years). Just over half of the patients were female (55.0%, *n*=220). The majority had moderate or severe acne at baseline, and most had a disease duration longer than 2 years. Baseline demographic and clinical characteristics are summarized in **Table 2**.

Treatment characteristics

Most patients were initiated on a daily dose of 0.4-0.7 mg/kg/day. The mean planned treatment duration was approximately 7 months, and the median cumulative dose approached 120 mg/kg. Treatment-related variables are presented in **Table 3**.

Overall incidence of adverse drug reactions

Of the 400 patients, 360 (90%) experienced at least one isotretinoin-related ADR during follow-up, while 40 (10%) had no documented ADR. Across the cohort, a total of 965 individual ADR events were recorded, reflecting that many patients experienced more than one reaction. Mucocuta-

Table 2. Baseline demographic and clinical characteristics (*n*=400)

Characteristic	Value
Age, years, mean ± SD	21.8±4.7
Age group, n (%)	
• 12–17 years	92 (23%)
• 18–24 years	214 (53.5%)
• ≥25 years	94 (23.5%)
Sex, *n* (%)	
• Male	180 (45%)
• Female	220 (55%)
Duration of acne, years, median (IQR)	3.0 (2.0–5.0)
Acne severity at baseline, *n* (%)	
• Mild	40 (10%)
• Moderate	232 (58%)
• Severe	128 (32%)
Comorbidities, *n* (%)	
• Any documented comorbidity	86 (21.5%)
• Baseline dyslipidemia	52 (13%)
• Known liver disease	10 (2.5%)
• Psychiatric history	14 (3.5%)
• Other (e.g. PCOS, thyroid disease)	24 (6%)
Concomitant medications, *n* (%)	
• Oral antibiotics (current/recent)	80 (20%)
• Hormonal therapy (females)	34 (8.5%)

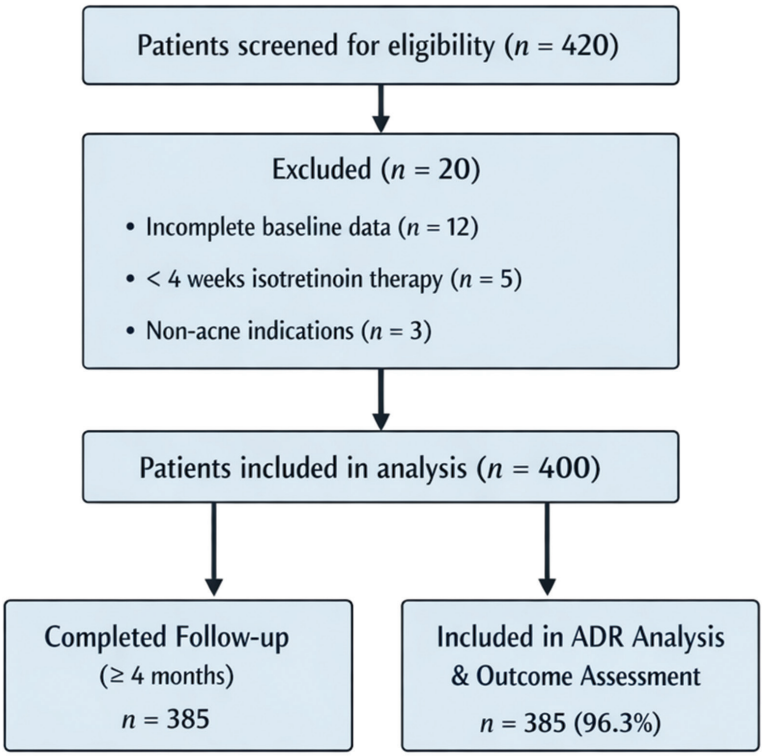

Figure 1. Flow diagram of patient selection and analysis.

Table 3. Isotretinoin treatment characteristics (*n*=400)

Treatment variable	Value
Starting dose, mg/kg/day, mean ± SD	0.52±0.12
Starting dose category, *n* (%)	
• <0.5 mg/kg/day	134 (33.5%)
• 0.5–0.7 mg/kg/day	214 (53.5%)
• >0.7 mg/kg/day	52 (13%)
Maximum daily dose, mg/kg/day, mean ± SD	0.63±0.15
Planned treatment duration, months, median (IQR)	7.0 (6.0–8.0)
Actual treatment duration, months, median (IQR)	6.8 (5.5–8.0)
Cumulative dose, mg/kg, median (IQR)	118 (95–140)
Cumulative dose category, *n* (%)	
• <100 mg/kg	132 (33%)
• 100–149 mg/kg	198 (49.5%)
• ≥150 mg/kg	70 (17.5%)

neous ADRs were the most common category, followed by laboratory abnormalities and systemic symptoms (mainly musculoskeletal). The overall incidence and distribution of ADRs are summarized in **Table 4**.

Table 4. Incidence and distribution of adverse drug reactions (n=400 patients; 965 ADR events)

Measure	Value
Patients with ≥1 ADR, ***n*** (%)	360 (90%)
Patients without ADR, ***n*** (%)	40 (10%)
Total ADR events, *n*	965
ADR events by category, *n* (%)	
• Mucocutaneous	730 (75.6%)
• Laboratory abnormalities	115 (11.9%)
• Musculoskeletal	75 (7.8%)
• Psychiatric	20 (2.1%)
• Gastrointestinal	15 (1.6%)
• Other (e.g. epistaxis not otherwise coded)	10 (1%)

Pattern of specific adverse drug reactions

Mucocutaneous ADRs

Mucocutaneous ADRs occurred in 354 patients (88.5%) and accounted for three-quarters of all recorded events. The most frequently observed were cheilitis and xerosis. The median time to onset of the first mucocutaneous ADR was 4 weeks (interquartile range 3–6 weeks) after starting isotretinoin **(Table 5)**.

Table 5. Mucocutaneous adverse drug reactions (per patient, *n*=400)

Mucocutaneous ADR	Patients affected ***n*** (%)
Cheilitis (dry, cracked lips)	344 (86%)
Xerosis of face / body	296 (74%)
Lip fissuring / eczema	160 (40%)
Facial erythema/dermatitis	80 (20%)
Dry eyes / conjunctival irritation	120 (30%)
Epistaxis (nasal dryness / bleeding)	104 (26%)
Hair thinning / telogen effluvium	60 (15%)

Most mucocutaneous reactions were graded as mild to moderate. Almost all patients were managed conservatively with intensive use of emollients, lip balms, and artificial tears. Dose reduction due to mucocutaneous toxicity alone was required in 52 patients (13%), and only 4 patients (1%) discontinued treatment permanently due to severe, intolerable mucocutaneous symptoms (e.g., painful fissuring, eczematous dermatitis not controlled with topical therapy) **(Figs 2, 3)**.

Laboratory abnormalities

Any treatment-emergent laboratory abnormality was documented in 88 patients (22%)—the most frequent changes involved serum triglycerides and liver enzymes. Many patients had overlapping abnormalities; therefore, the category totals exceed 22%. The distribution and severity of key laboratory abnormalities are shown in **Table 6**.

The majority of the abnormalities in the laboratory were asymptomatic and were identified during regular checks. Management involved dietary recommendations,

Table 6. Laboratory abnormalities during isotretinoin therapy (n=400)

Laboratory parameter and grade	Patients ***n*** (%)
Triglycerides	
• Mild elevation (≤2×ULN)	52 (13%)
• Moderate elevation (>2–3×ULN)	16 (4%)
• Severe elevation (>3×ULN)	4 (1%)
Total cholesterol	
• Mild elevation	24 (6%)
• Moderate elevation	8 (2%)
ALT/AST	
• Mild elevation (≤3×ULN)	18 (4.5%)
• Moderate elevation (>3×ULN)	6 (1.5%)
CBC abnormalities (e.g., leukopenia, thrombocytopenia)	6 (1.5%)

ULN: upper limit of normal; ALT: alanine aminotransferase; AST: aspartate aminotransferase; CBC: complete blood count

Folia Medica

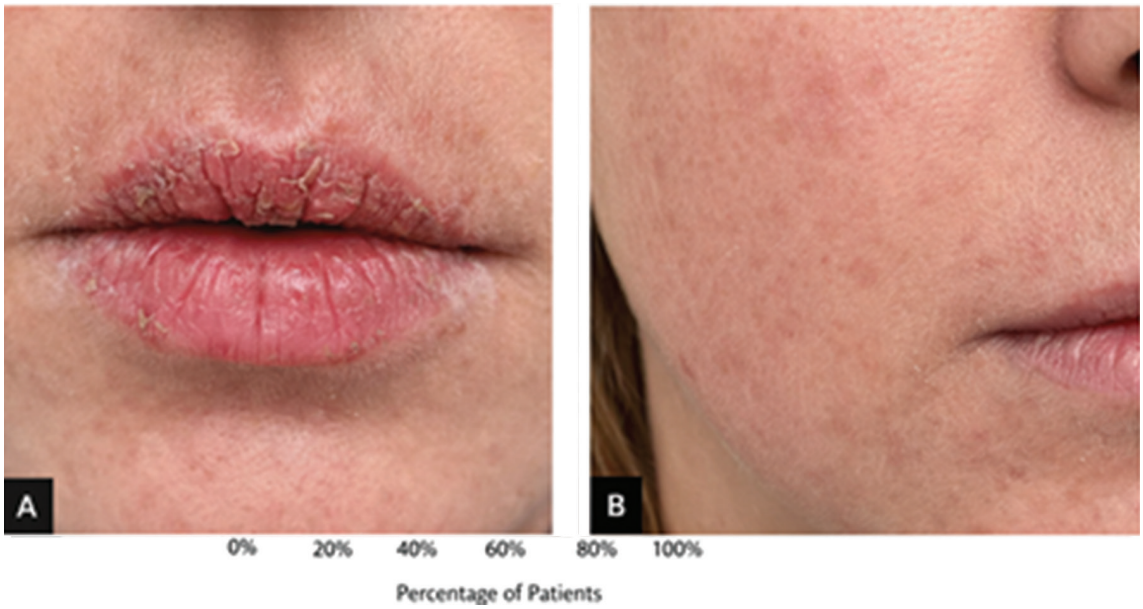

Figure 2. Representative mucocutaneous adverse drug reactions observed during isotretinoin therapy. Panel **A** illustrates cheilitis with fissuring and scaling of the lips, while panel **B** shows facial xerosis with mild erythema. These findings represent the most frequently documented adverse effects in the study cohort. Images are anonymized and published with patient consent.

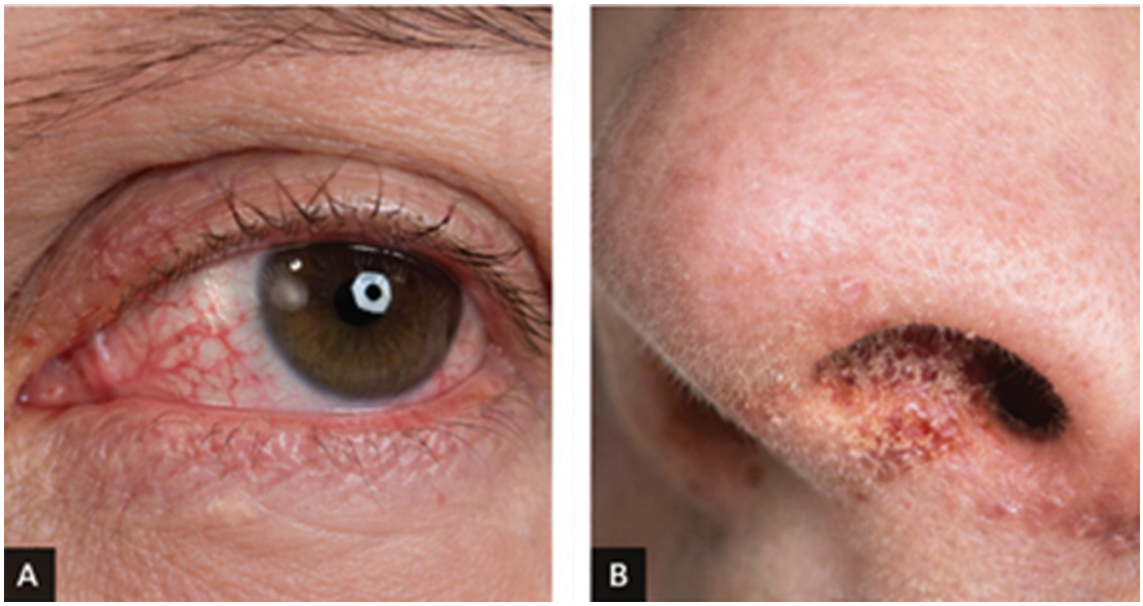

Figure 3. Ocular and nasal mucosal dryness associated with isotretinoin therapy, commonly presenting within the first weeks of treatment.

increased laboratory monitoring, and some minor dose modifications for mild abnormalities. In 22 cases (5.5%), moderate increases in lipids or liver enzymes led to a temporary decrease in dose or temporary withdrawal of the treatment. Four individuals with moderate hypertriglyceridemia (>3×ULN) and one with pronounced transaminitis were considered to have severe ADRs; isotretinoin was permanently discontinued in these individuals. None of the cases of clinically established acute pancreatitis were reported.

Systemic and other ADRs

Systemic (primarily musculoskeletal and neurological) ADRs occurred less frequently than mucocutaneous events but were clinically relevant in a subset of patients **(Table 7)**.

The majority of musculoskeletal complaints were mild or moderate and responded to simple analgesics and dose reduction. Isotretinoin use was temporarily interrupted in 12 patients (3.0%) due to musculoskeletal symptoms. Three of them had depressive symptoms of enough sever-

Table 7. Systemic and other adverse drug reactions (*n*=400)

Systemic/other ADR	Patients n (%)
Low back pain	64 (16%)
Generalized myalgia	52 (13%)
Arthralgia (large or small joints)	40 (10%)
Headache	36 (9%)
Gastrointestinal symptoms (nausea, dyspepsia, abdominal discomfort)	24 (6%)
Mood changes (e.g., low mood, irritability)	16 (4%)
Clinically significant depressive symptoms*	3 (0.75%)
Other (e.g., photosensitivity, fatigue)	14 (3.5%)

*Requiring psychiatric assessment and pharmacological intervention

ity to justify psychiatric referral; in two cases, isotretinoin was stopped, and the symptoms got better in the next few weeks. There were no records of suicide attempts or psychotic outbursts.

Severity and causality assessment

At the patient level, 220 patients (55%) experienced only mild ADRs, 110 (27.5%) had at least one moderate ADR (with or without additional mild reactions), and 30 (7.5%) had at least one severe ADR during the course of therapy. The remaining 40 patients (10%) had no ADR. At the event level, the distribution of severity for the 965 ADR events is shown in **Table 8**.

Table 8. Severity of adverse drug reactions (event-based, *n*=965)

Severity category	ADR events n (%)
Mild	690 (71.5%)
Moderate	230 (23.8%)
Severe	45 (4.7%)

Causality assessment using the Naranjo scale and WHO–UMC criteria indicated that the majority of ADRs were either definite or probable. A small number were deemed unlikely to be related to isotretinoin (e.g., intercurrent infections) and were excluded from specific analyses.

Factors associated with adverse drug reactions

For risk factor analysis, patients were grouped according to whether they experienced at least one moderate or severe ADR (*n*=140) or only mild or no ADRs (*n*=260). Baseline and treatment characteristics in these two groups are compared in **Table 9**.

In multivariable logistic regression, the dependent variable was the occurrence of at least one moderate/severe ADR. Variables entered into the model included sex, age, acne severity, baseline dyslipidemia, a daily dose of ≥0.5 mg/kg, and a cumulative dose of ≥120 mg/kg. The final model is presented in **Table 10**.

The model demonstrated acceptable calibration (Hosmer–Lemeshow p=0.63), higher daily dose, female sex, and baseline dyslipidemia were independently associated with an increased risk of moderate/severe ADRs.

Impact on treatment and clinical outcomes

ADR-related modifications to isotretinoin therapy were common but did not prevent most patients from completing a clinically effective course. Based on the most intensive action taken, treatment modifications are summarized in **Table 11 (Fig. 4)**.

Among the 16 patients who permanently discontinued isotretinoin due to ADRs, the main reasons were: severe laboratory abnormalities (*n*=8), severe refractory mucocutaneous symptoms (*n*=4), significant musculoskeletal pain (*n*=2), and clinically significant depression (*n*=2).

Table 9. Comparison of patients with versus without moderate/severe ADRs

Variable	Mild/none ADRs (*n*=260)	Moderate/severe ADRs (*n*=140)	*p*-value*
Age, years, mean ± SD	21.3±4.6	22.4±4.9	0.064
Female sex, *n* (%)	128 (49.2)	92 (65.7)	0.002
BMI, kg/m^2, mean ± SD	24.1±3.6	24.8±3.8	0.102
Severe acne at baseline, *n* (%)	74 (28.5)	54 (38.6)	0.041
Baseline dyslipidemia, *n* (%)	24 (9.2)	28 (20.0)	0.004
Psychiatric history, *n* (%)	6 (2.3)	8 (5.7)	0.092
Daily dose ≥0.5 mg/kg, *n* (%)	152 (58.5)	118 (84.3)	<0.001
Cumulative dose ≥120 mg/kg, *n* (%)	116 (44.6)	78 (55.7)	0.040
Treatment duration, months, median (IQR)	6.5 (5.5–7.5)	7.2 (6.0–8.5)	0.018

*p values derived from chi-square/Fisher's exact tests for categorical variables and t-test/Mann–Whitney U for continuous variables as appropriate.

Folia Medica

Table 10. Multivariable logistic regression for predictors of moderate/severe ADRs (*n*=400)

Predictor	Adjusted OR	95% CI	*p*-value
Female sex	1.82	1.15–2.88	0.011
Baseline dyslipidemia	2.15	1.18–3.91	0.012
Daily dose ≥0.5 mg/kg	3.05	1.85–5.02	<0.001
Severe acne at baseline	1.38	0.87–2.21	0.171
Cumulative dose ≥120 mg/kg	1.27	0.82–1.97	0.282
Age (per 1-year increase)	1.03	0.99–1.07	0.184

Table 11. Impact of ADRs on isotretinoin treatment (*n*=400)

ADR-related treatment modification	Patients *n* (%)
No ADR-related change	266 (66.5%)
Dose reduction only	90 (22.5%)
Temporary interruption (with later restart)	28 (7.0%)
Permanent discontinuation due to ADR	16 (4.0%)

Regarding clinical response, evaluation was available for 350 patients who completed at least 4 months of therapy; complete or near-complete clearance of acne lesions (≥90% reduction) was observed in 270/350 (77.1%). A good response (50%–89% reduction) occurred in 58/350 (16.6%), and a minimal response (<50% reduction) was documented in 22/350 (6.3%).

Discussion

The general incidence and trend of ADRs among this group are similar to those reported in the literature worldwide.[20] The meta-analytic and systematic review data show that mucocutaneous alterations, in particular, cheilitis and xerosis, are nearly universal in patients taking isotretinoin since they typically occur in more than 80-90% of treated people.[16,21] These frequencies (cheilitis 86%, xerosis 74%) are, in general, within this range and comparable to recent extensive real-world cohort studies in Europe and North America, in which mucocutaneous toxicity is the most consistent and predictable of all adverse-effect profiles of isotretinoin use.[22,23] The percentage of patients with any laboratory abnormality (22%) in Iraq is slightly higher than in particular Western series, where the clinical significance of lipid and liver enzyme increases is somewhat rare, and the results may not lead to any change.[17] Our results are consistent with the results of other areas that reveal that the measurable biochemical alterations, particularly hypertriglyceridemia, and mild transaminitis are not uncommon when using isotretinoin and are more common in patients with existing metabolic risk factors.[24] Most importantly, in such reports, severe hepatotoxicity was uncommon and recovered on dose reduction or withdrawal.[25]

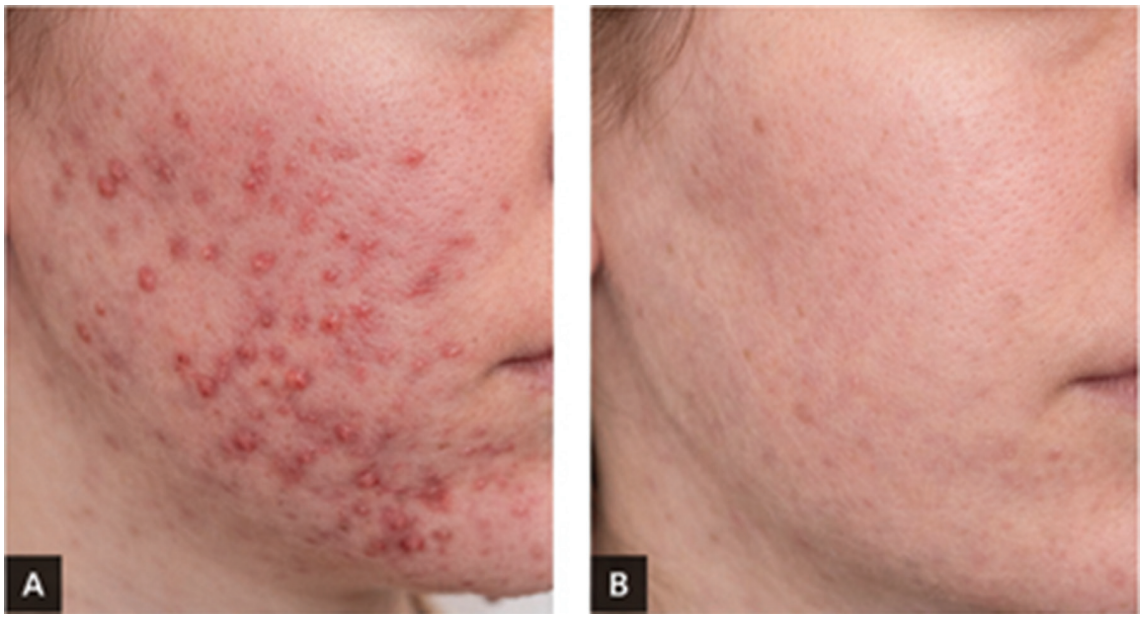

Figure 4. Clinical response to isotretinoin therapy showing marked reduction in inflammatory acne lesions after six months of treatment.

We also have similar rates of musculoskeletal symptoms and headache, which are also characterized by the literature of the time as low-grade back pain, arthralgia, and myalgia, which are frequent but generally mild complaints.[26] A recent meta-analysis of over 1.6 million study participants shows that the very low incidence of serious psychiatric outcomes in our cohort is consistent with no relative risk of suicide or psychiatric disorder among isotretinoin users compared with non-users and actually a decreased risk of suicide attempt at 2-4 years of follow-up.[27] Although reports of mood disturbance and suicidality at the individual level keep emerging[28], available evidence to date does not favor avoidance of isotretinoin in patients with a baseline psychiatric risk but instead close observation of said risk factors.

The current results also have significant clinical implications for the practice of dermatology in Iraqi clinics and other resource-limited settings. To begin with, the frequency of ADRs is high, specifically mucocutaneous symptoms and non-trivial abnormal biochemistry rates, which justify structured, protocol-based monitoring rather than informal or less rigid follow-up.[29,30] Metabolic status, liver disease, and psychiatric history must be systematically documented at baseline, and a regular lab test should be conducted within the initial 3 months of treatment, when most clinically significant abnormalities occur.[31,32] Meanwhile, our data and outside sources strongly indicate that really serious toxicity is uncommon, which is why a more risk-stratified monitoring paradigm will not require testing in low-risk individuals and will concentrate resources on patients with baseline dyslipidemia, high doses, or other comorbidities.[33,34]

Secondly, the independent correlations between moderate/severe ADRs and increased dose and persistently dyslipidemia indicate the relevance of dose individualization.[35] In the case of obese patients with a history of metabolic syndrome or excessive lipids, low-dose isotretinoin should be used, with a progressive increase in dosage and accompanied by explicit lifestyle counseling, to decrease the number of adverse events but still attain satisfactory levels of acne control, which is supported by real-world studies of low-dose regimens.[23,35] Integrating information on dose rationale, scheduled cumulative dose, and further modifications into clinical documentation would also be helpful for audit and continuous quality improvement.[27] Based on these results, several recommendations can improve pharmacovigilance and patient counseling regarding the use of isotretinoin in Iraq. At the service level, the use of a standardized isotretinoin monitoring checklist to measure baseline risk factors, lab tests, contraceptive counseling, mood screening, and ADR documentation would be beneficial for the dermatology practice. The addition of basic digital resources, such as SMS notifications for laboratory visits or follow-ups, might increase adherence to the monitoring regimen and reduce the risk of missed laboratory anomalies or undetected pregnancy.

At the system level, creating a local registry or electronic prescribing module for isotretinoin, including mandatory fields for pregnancy testing and contraception among women of reproductive age, may reflect some of the most important aspects of European PPPs and provide real-world evidence to guide policy. To confirm this, larger, multicenter, prospective studies in Iraq and neighboring nations should be conducted in the future to establish the variation in regional patterns of ADR and the cost-effectiveness of various approaches to monitoring.[16] Especially useful would be interventional studies that would test particular quality-improvement measures, i.e., structured checklists, electronic decision support, or specific laboratory protocols, as international evidence points to the fact that the currently used PPPs and monitoring practices are not yet perfect to prevent isotretinoin-related harm (Duran et al., 2023; Ivask et al., 2024). This would assist in aligning local practice with current global standards for the safe, effective, and patient-centered use of isotretinoin.

The proposed study has the prospective design and a relatively large sample size (n=400), which offers a complete description of isotretinoin safety in the practice of Iraqi clinics. But a number of limitations need to be noted: the study was done in 2 clinics of one city; it might be an insufficient number of clinics to make generalizations about the results. Moreover, the use of patient recollection of some of these symptoms, like mood changes, and the fact that no control group is used are also weaknesses of observational studies.

Conclusion

This report provides a detailed literature review of the safety of oral isotretinoin in common dermatological practice in Iraq. Adverse drug reactions were frequently experienced in a cohort of 400 patients, although serious events were few and could be predicted. Mucocutaneous responses, particularly cheilitis and xerosis, were nearly universal, and laboratory abnormalities and musculoskeletal complaints were present in a significant minority but were mild and reversible. Women were more prone to clinically significant toxicity. Patients with baseline dyslipidemia and those receiving their daily dose of at least 0.5 mg/kg were prone to clinically substantial toxicity, and close attention to the choice of patients and the individualization of doses is essential. Although the rate of adverse effects is high, the majority of patients received therapy with satisfactory clinical responses and high levels of treatment compliance, demonstrating that isotretinoin remains a handy option when properly monitored. Nevertheless, the potential for avoidable toxicity points to a need for continuous improvement in current monitoring and counseling practices. Enhancing organized clinical and laboratory surveillance, integrating systematic pregnancy prevention tools, and incorporating routine standardization of adverse reactions into daily practice might provide a significant improvement in medication safety. These findings need multicenter studies to confirm them and help create context-specific national guidelines.

References

1. Heng AHS, Chew FT. Systematic review of the epidemiology of acne vulgaris. Sci Rep 2020; 10:5754.
2. Layton AM, Bettoli V, Delore V, et al. The burden of acne vulgaris on health-related quality of life and psychosocial well-being domains: a systematic review. Am J Clin Dermatol 2025; 25(5):539–560.
3. Patel D, Thakre K, Badne P. Formulation and evaluation of *Psidium guajava*-enriched antioxidant face mask for anti-aging skin care. Med Pharm J 2025; 4:174–86.
4. Malik A. Psycho-social evaluation of University of Chenab students for HRQoL based on Acne-Specific Quality of Life Questionnaire (Acne-QoL). Int J Clin Stud Med Case Rep 2024; 47.
5. Sarwer DB, Siminoff LA, Gardiner HM, Spitzer JC. The psychosocial burden of visible disfigurement following traumatic injury. Front Psychol 2022; 13:979574.
6. Reynolds RV, Yeung H, Cheng CE, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol 2024; 90:1006.e1–1006.e30.
7. Leung AK, Barankin B, Lam JM, et al. Dermatology: how to manage acne vulgaris. Drugs Context 2021; 10:1–18.
8. Teichert M, Visser LE, Dufour M, et al. Isotretinoin use and compliance with the Dutch pregnancy prevention programme: a retrospective cohort study in females of reproductive age using pharmacy dispensing data. Drug Saf 2010; 33:315–26.
9. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol 2016; 74(5):945–73.e33.
10. Feszak IJ, Brzeziński P, Feszak S, et al. Isotretinoin treatment for acne vulgaris: a five-year retrospective analysis of clinical and biochemical adverse effects. J Clin Med 2025; 14:6473.
11. Rajput I, Anjankar VP. Side effects of treating acne vulgaris with isotretinoin: a systematic review. Cureus 2024;16(3):e55946. doi: 10.7759/cureus.55946.
12. Ding RL, Zheng Y, Bu J. Physiological and psychological effects of isotretinoin in the treatment of patients with acne: a narrative review. Clin Cosmet Investig Dermatol 2023; 16:1843–54.
13. Szilagyi DV, Tit DM, Judea-Pusta CT, et al. Real-world evidence of neuropsychiatric adverse reactions to isotretinoin: insights from EudraVigilance (2005–2025). Pharmaceuticals (Basel) 2025; 18:1252.
14. Ruchitha S, Gupta N, Singh K. Exploring the multifaceted side effects of isotretinoin: a deep dive into case reports and observational studies. Arch Dermatol Res 2025; 317:499.
15. Paljarvi T, McPherson T, Luciano S, et al. Isotretinoin and adverse neuropsychiatric outcomes: retrospective cohort study using routine data. Br J Dermatol 2022; 187:64–72.
16. Kapała J, Lewandowska J, Placek W, et al. Adverse events in isotretinoin therapy: a single-arm meta-analysis. Int J Environ Res Public Health 2022; 19:6463.
17. Barbieri JS, Shin DB, Wang S, et al. The clinical utility of laboratory monitoring during isotretinoin therapy for acne and changes to monitoring practices over time. J Am Acad Dermatol 2020; 82:72–9.
18. Lee KWA, Chan LKW, Lee CH, et al. Idiosyncratic reaction of isotretinoin: a review. Dermatol Rev 2024; 5:e70001.
19. Jha A, Shrestha R, Khadka A, et al. Effect of low-dose isotretinoin on lipid profile and liver enzymes in acne patients: a cross-sectional study. Nepal J Dermatol Venereol Leprol 2024; 22:28–31.
20. Narayanan D, Rogge M. Cheilitis: a diagnostic algorithm and review of underlying etiologies. Dermatitis 2024; 35:431–42.
21. Metin N, Karapınar T, Turan Ç. Lip mesotherapy with dexpanthenol in the treatment of isotretinoin-induced cheilitis. J Cosmet Dermatol 2022; 21:4684–90.
22. Sibi Krishna T, Kaur R, Malhotra V, et al. The impact of isotretinoin on lipid profile: a systematic review. Ann Med Surg (Lond) 2025; 87:4395–403.
23. Reyes-Hadsall S, Ju T, Keri JE. Use of oral supplements and topical adjuvants for isotretinoin-associated side effects: a narrative review. Skin Appendage Disord 2024; 10:1–9.
24. Bazargan AS, Jafarzadeh A, Danandeh F, et al. Investigating metabolic syndrome markers and body mass index changes in patients with acne vulgaris treated with isotretinoin: a prospective study. J Cosmet Dermatol 2024; 23:4343–8.
25. Tawanwongsri W, Kanchanasuwan T, Eden C. Isotretinoin and hepatotoxicity in patients with acne: a narrative review. Cosmetics (Basel) 2025; 12:17.
26. Rademaker M. Isotretinoin: dose, duration and relapse. What does 30 years of usage tell us? Australas J Dermatol 2013; 54(3):157-62.
27. Tan NKW, Tang A, MacAlevey NCYL, et al. Risk of suicide and psychiatric disorders among isotretinoin users: a meta-analysis. JAMA Dermatol 2024; 160:54.
28. Schaffer LC, Schaffer CB, Hunter S, et al. Psychiatric reactions to isotretinoin in patients with bipolar disorder. J Affect Disord 2010; 122:306–8.
29. Patrzykąt KM, Puchalski K, Liszka P, et al. Beyond clinical efficacy: a literature review on the safety challenges of isotretinoin therapy. Qual Sport 2025; 48:67344.
30. Kaya K, Gevher Ö. Isotretinoin increases non-insulin-based surrogate markers of insulin resistance in acne vulgaris patients. Cutan Ocul Toxicol 2024; 43:410–5.
31. Turan Ç, Öner Ü. Lip mesotherapy with dexpanthenol as a novel approach to prevent isotretinoin-associated cheilitis. Dermatol Pract Concept 2023; e2023012.
32. Landis MN. Optimizing isotretinoin treatment of acne: update on current recommendations for monitoring, dosing, and relapse prevention. Am J Clin Dermatol 2020; 21(3):411–28.
33. Paichitrojjana A, Paichitrojjana A. Oral isotretinoin and its uses in dermatology: a review. Drug Des Devel Ther 2023; 17:2573–91.
34. Muhaidat J, Alhuneafat L, Asfar R, et al. Exploring the incidence and risk factors of dyslipidemia in patients with severe acne vulgaris on systemic isotretinoin therapy: findings from a prospective study. Medicina (Kaunas) 2025; 61:439.
35. Kandhari R. Isotretinoin: an updated review on the profile of its side-effects and their management. Egypt J Dermatol Venereol 2023; 43:1–7.

Additional information

Ethical statement

- The authors declared that no clinical trials were used in the present study.
- The authors declared that no experiments on humans or human tissues were performed for the present study.
- Written informed consent was obtained from all participants or their guardians for minors for anonymized patient information and publication of any accompanying images. The signed informed consent forms are safely deposited at the Iraqi Medical Research Center, Bagdad and are securely stored to protect patient privacy.
- The study protocol was reviewed and approved by the Institutional Review Board of the College of Pharmacy at the University of Basra (Approval No. 238/2022). The study was conducted in accordance with the Declaration of Helsinki.
- The authors declared that no experiments on animals were performed for the present study.
- The authors declared that no commercially available immortalized human and animal cell lines were used in the present study.

Conflict of interest

The authors declare no conflict of interest regarding the publication of this study.

Artificial Intelligence (AI) use

The authors accept full responsibility for the content of the manuscript, including the disclosure of any use of AI. No AI tools were used in the preparation of this manuscript.

Funding

All authors declare that they received no financial support from any institution or university.

Author contributions

All authors have contributed equally.

Author ORCIDs

Qutaiba Qasim https://orcid.org/0000-0001-9566-0850
Jubran Hassan https://orcid.org/0000-0003-0813-5260
Kadhim Ali Kadhim https://orcid.org/0000-0002-4040-1808
Hany Akeel Al-hussaniy https://orcid.org/0000-0003-2647-8574

Data availability

All data used are referenced or included in the article.