

Adverse Events During Oral Isotretinoin Therapy a Prospective Hospital Based Descriptive Study**B. Rekha Rani¹, N. Krishna Sagar², V. Jyothi³, K.V.T. Gopal⁴**¹Assistant Professor, Department of Dermatology Venerology and Leprosy, Maharajah Institute of Medical Sciences (MIMS), Vizianagaram, Andhra Pradesh, India²Assistant Professor, Department of Dermatology Venerology and Leprosy, Maharajah Institute of Medical Sciences (MIMS), Vizianagaram, Andhra Pradesh, India³Consultant, Department of Dermatology Venerology and Leprosy, Maharajah Institute of Medical Sciences (MIMS), Vizianagaram, Andhra Pradesh, India⁴Professor and Head, Department of Dermatology Venerology and Leprosy, Maharajah Institute of Medical Sciences (MIMS), Vizianagaram, Andhra Pradesh, India

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Abstract**Background:** Oral isotretinoin is effective for acne and selected keratinization disorders, but treatment requires surveillance for clinical and laboratory adverse events.**Objectives:** To describe dermatological, ophthalmic, psychiatric, menstrual and laboratory events during isotretinoin therapy and their reported timing.**Methods:** A prospective descriptive study enrolled 60 dermatology outpatients at Maharajah's Institute of Medical Sciences, Nellimarla, Andhra Pradesh, between December 2016 and May 2018. Patients received isotretinoin at a fixed dose of 20 mg daily. Baseline evaluation included clinical examination, ophthalmic testing, Hamilton anxiety and depression assessments, and laboratory investigations. Follow-up was scheduled at months 1, 2, 3 and 6. Findings were summarized as frequencies and percentages.**Results:** Participants comprised 36 males (60.0%) and 24 females (40.0%); mean age was 23.16 years. Acne accounted for 52 prescriptions (86.7%). Cheilitis occurred in 37 patients (61.7%), cutaneous xerosis and hair loss in 24 each (40.0%), and reduced tear production in 20 (33.3%). Corneal xerosis affected 10 patients (16.7%) and blurred vision six (10.0%). Depression was recorded in seven patients (11.7%); anxiety and suicidal ideation were not reported. Menstrual irregularities occurred in eight of 24 females (33.3%). Headache affected 20 patients (33.3%); elevated triglycerides and alkaline phosphatase were recorded in four (6.7%) and one (1.7%), respectively. Mucocutaneous symptoms appeared early, while several other events were documented around the third month.**Conclusion:** Mucocutaneous and ocular findings predominated. Hair loss, depressive symptoms and menstrual disturbances warrant attention during follow-up. The uncontrolled design establishes observed event frequencies rather than drug-attributable risks.**Keywords:** Isotretinoin; Adverse Events; Cheilitis; Dry Eye; Depression; Menstrual Irregularities; Pharmacovigilance.**DOI:** 10.25258/ijcpr.18.10.72

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Introduction

Acne vulgaris is an inflammatory disorder of the pilosebaceous unit that presents with comedones, papules, pustules and, in more severe disease, nodules and scarring. Its consequences extend beyond visible lesions to psychological distress and impaired daily functioning. Oral isotretinoin remains an important treatment for severe acne, acne associated with scarring or substantial psychosocial burden, and disease unresponsive to standard therapy. Contemporary guidelines place

treatment selection within an individualized assessment of clinical severity, prior response and patient needs.[1] Understanding tolerability is therefore essential when translating therapeutic benefit into sustained treatment. Isotretinoin influences several processes involved in acne, including sebaceous activity, follicular keratinization and inflammation. These actions explain its distinctive clinical role, but systemic exposure also affects tissues outside the

pilosebaceous unit. Dose selection, treatment duration and counselling shape prescribing decisions.[2] Adverse-event syntheses identify a broad spectrum of manifestations, with mucocutaneous complaints prominent across clinical studies.[3] Cheilitis and xerosis are often readily recognized, whereas hair shedding, visual symptoms and disturbances affecting other systems require deliberate questioning. Reporting individual events separately is useful because one patient can experience several manifestations during the same course.

Ocular surveillance deserves particular attention because tear-film disturbance can produce discomfort and interfere with vision. A systematic review identified dry eye as the most frequently reported ocular effect, alongside less common inflammatory and visual findings.[4] Psychiatric outcomes require a different interpretive approach: acne itself contributes to emotional burden, and symptoms recorded during treatment do not automatically demonstrate pharmacological causation. A large meta-analysis found no population-level increase in psychiatric risk while supporting continued clinical attention to mental health.[5] Baseline assessment and repeated review are consequently valuable components of an observational safety study.

Laboratory changes also influence follow-up. Published evidence distinguishes measurable biochemical shifts from abnormalities that require intervention, and a meta-analysis questioned routine monthly testing in otherwise standard acne populations.[6] An international Delphi study subsequently supported targeted alanine aminotransferase and triglyceride testing at baseline and peak dose.[7]

Other outcomes receive less consistent surveillance. Hair-loss frequencies vary across studies and dosing categories,[8] while prospective evidence has documented menstrual disturbances during isotretinoin treatment.[9] These findings justify recording symptoms alongside laboratory results, using explicit denominators and avoiding unsupported comparisons between populations.

Local prospective observations can describe the clinical pattern encountered in routine dermatology practice, particularly when prescriptions include both acne and keratinization disorders. Repeated specialist examinations offer an opportunity to identify events that symptom reporting alone overlooks. However, descriptive follow-up cannot separate treatment effects from background illness without a comparison group. The objectives of this study were to describe the dermatological, ophthalmic and psychiatric event profile among patients receiving oral isotretinoin; document menstrual disturbances, other systemic complaints

and laboratory abnormalities; and characterize the reported timing of these findings during treatment.

Methodology

Study Design and Setting: This prospective hospital based descriptive study was conducted in the Department of Dermatology, Venereology and Leprology at Maharajah's Institute of Medical Sciences and its general hospital, Nellimarla, Vizianagaram district, Andhra Pradesh. The study period extended from December 2016 to May 2018. Sixty patients prescribed oral isotretinoin for acne vulgaris, disorders of keratinization or other dermatoses constituted the study cohort. Treatment was selected clinically rather than assigned through randomization; no untreated or alternative-treatment comparator was included.

Eligibility and Treatment Exposure: The protocol permitted patients of all ages receiving isotretinoin at doses of at least 20 mg/day. Patients received a fixed regimen of 20 mg once daily, irrespective of body weight. Exclusions comprised pregnancy risk, lactation, noncompliance with contraception, abnormal baseline lipid, liver or renal profiles, known diabetes mellitus, use of drugs described as hyperlipidaemic, and systemic antibiotics or isotretinoin during the preceding six months. The cohort size was descriptive; a formal sample-size calculation was not documented.

Baseline Clinical and Laboratory Assessment: After informed consent, demographic characteristics, weight, disease duration, age at onset, personal and family history, and previous treatment were recorded. General and systemic examinations were performed, together with menstrual history in female participants. Dermatological assessment established the diagnosis and graded acne where applicable. Participants received counselling regarding their disease and prescribed medication. Baseline investigations comprised complete haemogram, fasting blood glucose, lipid profile, liver function tests and renal function tests.

Specialist Assessment and Follow-up: Ophthalmic evaluation included visual acuity, slit-lamp examination, intraocular pressure by applanation and noncontact tonometry, fundoscopy, indirect ophthalmoscopy and Schirmer testing. Psychiatric assessment used the Hamilton Anxiety Rating Scale and Hamilton Depression Rating Scale at the psychiatry outpatient department.[10,11] The same physician performed psychiatric assessments. Follow-up visits were scheduled at months 1, 2, 3 and 6. At each visit, patients were questioned specifically about dermatological, ocular, psychiatric and other systemic symptoms and asked to classify reported severity as mild, moderate or severe.

Dermatological, ophthalmic and psychiatric examinations and laboratory investigations were repeated.

Outcomes and Statistical Analysis: Outcomes were the reported clinical events, laboratory abnormalities and their temporal pattern. Analysis was descriptive, using counts and percentages. The denominator was 60 except for menstrual outcomes, which used the 24 female participants. Percentages were calculated from event counts and rounded to one decimal place.

Events were nonexclusive. Timing was summarized narratively because visit-specific counts were unavailable; no correlation

coefficients, hypothesis tests or adjusted causal estimates were calculated.

Ethical Considerations: The study was approved by the institutional ethics committee. Informed consent was obtained from participants before study procedures.

Results

Participant Characteristics and Treatment Indications: The analysis included 60 patients: 36 males (60.0%) and 24 females (40.0%). Mean age was 23.16 years. The largest reported age group was 15–25 years, comprising 43 participants (71.7%) (Table 1).

Table 1: Demographic characteristics of the study population

Characteristic	n	%
Male	36	60.0
Female	24	40.0
Age 15–25 years	43	71.7
Age 25–35 years	13	21.7
Age 35–45 years	4	6.7

Note. N = 60. Mean age was 23.16 years; standard deviation was not reported. Reported age bands contain overlapping boundary ages.

Acne vulgaris accounted for 52 prescriptions (86.7%), including 26 patients with grade IV acne. Eight patients (13.3%) received isotretinoin for other dermatoses (Table 2).

Table 2: Indications for isotretinoin treatment

Indication	n	%
Acne vulgaris grades I–II	11	18.3
Acne vulgaris grade III	15	25.0
Acne vulgaris grade IV	26	43.3
Ichthyosis	3	5.0
Focal keratoderma	2	3.3
Erythrokeratoderma variabilis	2	3.3
Porokeratosis	1	1.7

Note. N = 60. Acne grades I–II were combined in the source. Percentages refer to the entire cohort.

Cutaneous and ophthalmic findings: Cheilitis was the most frequently recorded cutaneous event, affecting 37 patients (61.7%). Cutaneous xerosis and hair loss were each reported in 24 patients (40.0%). Photosensitivity was recorded in six patients (10.0%) (Table 3). No treatment discontinuations attributable to cutaneous events were reported.

Table 3: Cutaneous events recorded during treatment

Event	n	%
Cheilitis	37	61.7
Cutaneous xerosis	24	40.0
Hair loss or alopecia	24	40.0
Photosensitivity	6	10.0

Note. N = 60. Individual events were nonexclusive; their counts cannot be summed to estimate patients with any cutaneous event.

At least one ophthalmic finding was recorded in 23 patients (38.3%). Reduced tear production on Schirmer testing was the most frequent finding (20 patients; 33.3%), followed by corneal xerosis (10; 16.7%). Blurred vision was recorded in six patients (10.0%) (Table 4).

Table 4: Ophthalmic findings recorded during treatment

Finding	n	%
Any ophthalmic finding	23	38.3
Reduced tear production	20	33.3
Corneal xerosis	10	16.7
Blurred vision	6	10.0
Refractive changes	3	5.0
Blepharitis	2	3.3
Amblyopia	1	1.7

Note. N = 60. Findings overlap. Amblyopia is retained as a recorded finding; new onset and causal attribution were not established.

Psychiatric and menstrual outcomes: Depression was recorded in seven patients (11.7%). Anxiety and suicidal ideation were not reported (Table 5). Numerical baseline and follow-up Hamilton scores and severity-category counts were unavailable.

Table 5: Psychiatric outcomes recorded during treatment

Outcome	n	%
Depression	7	11.7
Anxiety	0	0.0
Suicidal ideation	0	0.0

Note. N = 60. Absence of reported events does not establish absence of risk. Depression classification thresholds were not supplied.

Menstrual irregularities were recorded in eight of the 24 female participants (33.3%). Amenorrhea affected five females (20.8%), and oligomenorrhea affected three (12.5%) (Table 6).

Table 6: Menstrual outcomes among female participants

Outcome	n	%
Any menstrual irregularity	8	33.3
Amenorrhea	5	20.8
Oligomenorrhea	3	12.5

Note. Denominator = 24 females. Any menstrual irregularity affected 13.3% of the entire cohort. Menarchal status and contraceptive exposure were not separately tabulated.

Other clinical events and laboratory abnormalities: Headache was reported by 20 patients (33.3%); myalgia occurred in one (1.7%). Increased triglycerides were recorded in four patients (6.7%), and increased alkaline phosphatase in one (1.7%) (Table 7). Absolute biochemical values and laboratory grading were not available.

Table 7: Other clinical events and laboratory abnormalities

Event or abnormality	n	%
Headache	20	33.3
Myalgia	1	1.7
Increased triglycerides	4	6.7
Increased alkaline phosphatase	1	1.7

Note. N = 60. The magnitude, reference thresholds and clinical consequences of laboratory elevations were not reported.

Temporal pattern of reported events: Cheilitis, xerosis and headache were described within the first month. Corneal xerosis, blepharitis and photosensitivity appeared at approximately 6–8 weeks. Hair loss, depression, visual or refractive symptoms and triglyceride elevation were described around 12 weeks. Menstrual disturbances

were reported after approximately 8–12 weeks, while alkaline phosphatase elevation was documented at six months (Table 8).

These descriptions do not constitute a statistical association with treatment duration.

Table 8: Reported timing of events during isotretinoin treatment

Reported interval	Events described
First month	Cheilitis, cutaneous xerosis and headache
Approximately 6–8 weeks	Corneal xerosis, blepharitis and photosensitivity
Approximately 8–12 weeks	Menstrual irregularities
Approximately 12 weeks	Hair loss, depression, refractive changes, blurred vision and increased triglycerides
Six months	Increased alkaline phosphatase

Note. Timing reflects narrative descriptions rather than patient-level onset data. Photophobia was listed at month 2 without a corresponding event count.

Discussion

This prospective cohort documented a predominance of mucocutaneous and ocular findings during isotretinoin treatment. Cheilitis affected 61.7% of participants, while xerosis and hair loss each affected 40.0%. These observations support the practical importance of symptom counselling and repeated clinical assessment. Nevertheless, frequency alone does not establish drug causation. The cohort included different dermatological indications, and its descriptive design did not account for underlying disease, concomitant exposures or individual susceptibility. The results therefore describe this clinical population rather than a comparative estimate of isotretinoin toxicity.

The prominence of cheilitis and xerosis agrees with the overall adverse-event pattern reported in clinical syntheses.[3,12] Rademaker's larger retrospective series likewise documented common mucocutaneous complaints and clinically relevant tolerability problems.[13] The present hair-loss proportion is particularly notable: Lytvyn and colleagues reported frequencies of 3.2% with doses below 0.5 mg/kg/day and 5.7% with higher doses.[8] Differences in ascertainment, disease mix and outcome definition complicate comparison. Without standardized hair evaluation or weight-adjusted exposure, the 40.0% figure cannot be interpreted as a dose effect or confirmed telogen effluvium. Ophthalmic findings affected 38.3% of participants, predominantly reduced tear production and corneal xerosis. Their pattern is consistent with the ocular surface disturbance described by Lamberg and colleagues.[4] Baseline examination and repeat Schirmer testing were useful features of the protocol. However, thresholds and paired numerical results were unavailable, limiting assessment of clinical magnitude. Blurred vision warrants specialist evaluation, while the isolated amblyopia entry requires caution because its onset was not established. Early dryness and later visual complaints indicate the value of asking about ocular symptoms throughout treatment rather than only at initiation.

Depression was recorded in 11.7%, without reported anxiety or suicidal ideation. These findings do not resolve the debated psychiatric association because baseline symptom distributions and diagnostic cutoffs were unavailable. Tan and colleagues found no population-level increase in psychiatric risk across a large evidence base,[5] whereas recent pharmacovigilance analysis identified reporting signals that support continued surveillance.[14] Spontaneous-report signals are not incidence estimates. Taken together, the evidence supports baseline mental-health

assessment and attention to emerging symptoms, without attributing every depressive presentation to isotretinoin.

Menstrual irregularities affected one-third of female participants, highlighting an outcome easily overlooked during routine review. Prospective research has also documented menstrual changes during exposure.[9] Interpretation here is restricted by absent contraceptive and endocrine data.

Triglyceride elevation occurred in 6.7%, while alkaline phosphatase elevation was uncommon. These observations align with the need to distinguish laboratory changes from clinically important toxicity.[6,7] The reported timing supports ongoing follow-up, but visit-specific denominators were unavailable. Individualized surveillance should address symptoms and relevant laboratory findings; this small cohort cannot determine an optimal monitoring schedule or establish overall treatment safety.

Limitations

The single-centre cohort was small, uncontrolled and heterogeneous in treatment indication. Fixed dosing prevented assessment of weight-adjusted exposure. Visit-specific attendance, cumulative doses, laboratory thresholds, numerical psychiatric scores and standardized causality assessments were unavailable. Menstrual outcomes lacked contraceptive and endocrine adjustment. Age categories overlapped at their boundaries. These constraints restrict causal inference, duration-based comparisons, detection of rare events and generalization beyond the studied outpatient population.

Conclusion

In this prospective cohort of 60 isotretinoin-treated patients, cheilitis, xerosis, hair loss and reduced tear production were prominent findings. Depression was recorded in seven patients, and menstrual irregularities affected eight of 24 females. Laboratory abnormalities were less frequent than clinical complaints. The reported temporal pattern indicates that surveillance should continue beyond the first month, with attention to ocular symptoms, mood changes and menstrual history alongside mucocutaneous tolerability. These results provide descriptive evidence from dermatology practice, but they do not establish drug-attributable risks or exclude uncommon serious reactions.

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