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A Prospective Study on Clinical Efficacy of Oral Isotretinoin in Moderate To Severe Acne Vulgaris with Effects on Liver Enzymes and Lipid Profile in A Tertiary Care Hospital

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Conflict of interest: Nil

Abstract

Background: Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit, predominantly affecting adolescents and young adults. Oral isotretinoin has revolutionized the treatment of moderate to severe acne by targeting all major pathogenic mechanisms.

Aim and Objectives: This study aimed to evaluate the clinical efficacy of low-dose oral isotretinoin in patients with moderate to severe acne vulgaris, while monitoring changes in lipid profile, liver enzymes, and documenting adverse effects.

Materials and Methods: A hospital based prospective study was conducted from September to December 2024 in the DVL outpatient department of Santhiram Medical College and General Hospital, Nandyal, Andhra Pradesh. Thirty patients aged 18–30 years with clinically diagnosed Grade III/IV acne were administered oral isotretinoin at 0.2 mg/kg/day for four months. Acne severity was assessed using the Leeds grading system. Lipid profile (TC, TG, HDL, LDL) and liver enzymes (AST, ALT) were evaluated at baseline, 2 months, and 4 months. Adverse events were recorded throughout the study.

Results: Significant clinical improvement was observed in acne severity, with 53.3% of patients achieving Grade I acne by the end of treatment. Cheilitis (56.6%) was the most common adverse effect, followed by xerosis (33.3%) and mucocutaneous dryness. Statistically significant increases were noted in total cholesterol ($P<0.05$), triglycerides ($P<0.05$), and LDL ($P<0.05$), while HDL levels significantly decreased ($P<0.05$). AST and ALT levels remained within normal limits and were not significantly altered ($P>0.05$).

Conclusion: Low-dose oral isotretinoin (0.2 mg/kg/day) is effective in reducing acne severity in young adults with moderate to severe acne, with manageable side effects. While lipid abnormalities were commonly observed, liver function remained unaffected, highlighting the importance of regular biochemical monitoring during therapy.

Keywords: Acne vulgaris, isotretinoin, low-dose, lipid profile, liver enzymes, adverse effects, Leeds grading system.

Introduction

Acne vulgaris is a chronic inflammatory condition of the pilosebaceous unit, predominantly affecting adolescents and young adults. It typically manifests on the face, and to a lesser extent, on the back and chest. Clinically, it presents with seborrhoea, open and closed comedones, erythematous papules, pustules, and in more severe cases, nodules, deep pustules, pseudocysts, and subsequent scarring.[1]

Management of acne depends on its severity and includes both topical and systemic treatments. Among systemic options, oral antibiotics and oral isotretinoin are widely used. Isotretinoin is considered one of the most significant advancements in the treatment of acne.[2]

Oral isotretinoin (13-cis-retinoic acid), a synthetic derivative of vitamin A, has transformed the therapeutic approach for treatment-resistant acne. It acts on all four major pathogenic mechanisms of acne: normalizing abnormal follicular keratinization, reducing sebum production by approximately 70% through inhibition of sebocyte differentiation, diminishing colonization by cutibacterium acnes (formerly Propionibacterium acnes), and exerting anti-inflammatory effects.[3]

The standard dosage ranges from 0.5 to 1.0 mg/kg/day, administered over 16 to 32 weeks, aiming for a cumulative dose of up to 120 mg/kg.[4] However, its use is associated with various adverse effects, including cheilitis, xerosis, and alterations in lipid profile and liver enzymes. Therefore, thorough patient counselling, baseline investigations, and regular monitoring of lipid parameters and liver function tests are essential throughout treatment.[5]

Aim of the Study

This study is designed to assess the clinical effectiveness of oral isotretinoin in patients with moderate to severe acne vulgaris.

Objectives: Evaluating the reduction in acne severity using the Leeds grading system, monitoring changes in lipid profile parameters (total cholesterol, triglycerides, HDL, and LDL), assessing liver function via serum levels of AST and ALT, and documenting any adverse effects observed during the course of therapy.

Materials and Methods

This hospital based prospective study was carried out in the DVL outpatient department of Santhiram Medical College and General Hospital, Nandyal, Andhra Pradesh, from September to December 2024. The study was approved by Institutional Ethics Committee and written informed consent was taken from all patients .The study population included both male and female patients aged 18 to 30 years who had a clinical diagnosis of acne. Individuals who declined to participate, those with hyperlipidemia undergoing statin therapy, and patients with photosensitive disorders were excluded from the study.

Patients presenting with moderate to severe acne vulgaris (Grade III and Grade IV) were enrolled in the study following the acquisition of written informed consent. Data were collected using a structured proforma, which captured detailed medical history, findings from

cutaneous and systemic examinations, and relevant laboratory investigations, including liver function tests and lipid profile. A urine pregnancy test was performed for all female participants of reproductive age prior to initiating isotretinoin therapy. All enrolled patients received low-dose oral isotretinoin at a dosage of 0.2 mg/kg/day for a duration of four months. Treatment efficacy was evaluated through standardized clinical photography and assessed using the Leeds grading system.

Statistical analysis

The data obtained were analysed statistically using SPSS software version 23. Correlation between variables was calculated using Chi-square test. P-value < 0.05 was considered statistically significant.

Table 1: Leeds Grading System for Acne Severity

Grade	Description
Grade I	**Mild acne:** Predominantly comedones (blackheads and whiteheads), few small papules, minimal inflammation.
Grade II	**Moderate acne:** More numerous papules and pustules, some comedones, mild to moderate inflammation.
Grade III	**Moderately severe acne:** Numerous papules, pustules, occasional nodules, moderate to severe inflammation, widespread distribution.
Grade IV	**Severe acne:** Predominantly large, painful nodules and cysts, severe inflammation, extensive involvement with risk of scarring.

Treatment response and monitoring of lipid profile and liver enzyme levels were carried out at baseline, at the end of the second month, and at the end of the fourth month. Total cholesterol levels were categorized as normal (<200 mg/dL), borderline high (200–239 mg/dL), high (≥ 240mg/dL), and very high (≥300 mg/dL). Triglyceride levels were classified as normal (<150 mg/dL), borderline high (150–199 mg/dL), high (200–499 mg/dL), and very high (≥500 mg/dL). High-density lipoprotein (HDL) levels were considered low if <40 mg/dL, normal between 40–59 mg/dL, and high if ≥60 mg/dL. Low-density lipoprotein (LDL) levels were defined as optimal (<100 mg/dL), above optimal (100–129 mg/dL), borderline high (130–159 mg/dL), high (160–189 mg/dL), and very high (≥190 mg/dL). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) values were interpreted as normal if <40 U/L and elevated if ≥40 U/L.

Clinical efficacy was assessed at each follow-up visit by evaluating the reduction in both the number and size of acne lesions. All participants tolerated low-dose oral isotretinoin well, adhered to the treatment regimen, and none discontinued the study.

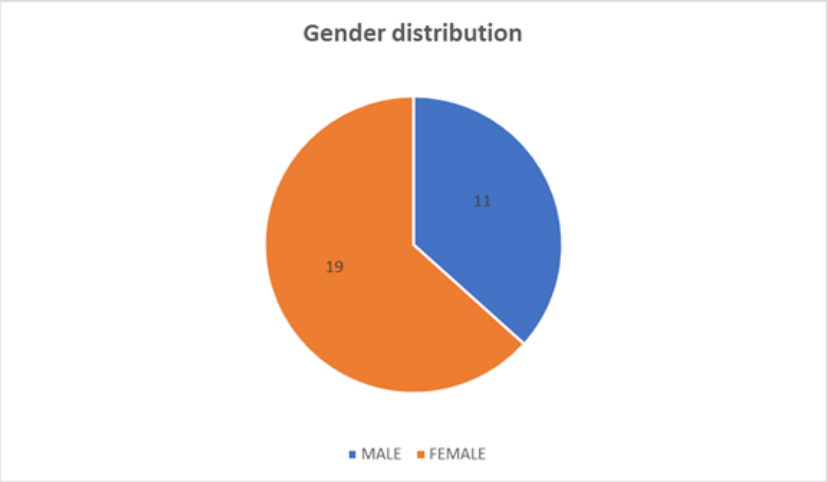
Results

A total of 30 participants aged between 18 and 30 years were enrolled in the study. Among them, 19 (60%) were female and 11 (40%) were male. The mean age of the male participants was 23.8 ± 3.6 years, whereas the mean age of the female participants was 22.4 ± 3.2 years.

Table 2: Age, sex and Grades of participants

Sex	N(%)	Mean age	Moderate	Severe
Male	11(40%)	23.8±3.4	5	6
Female	19(60%)	22.47±3.2	7	12

Graph 1: Gender distribution

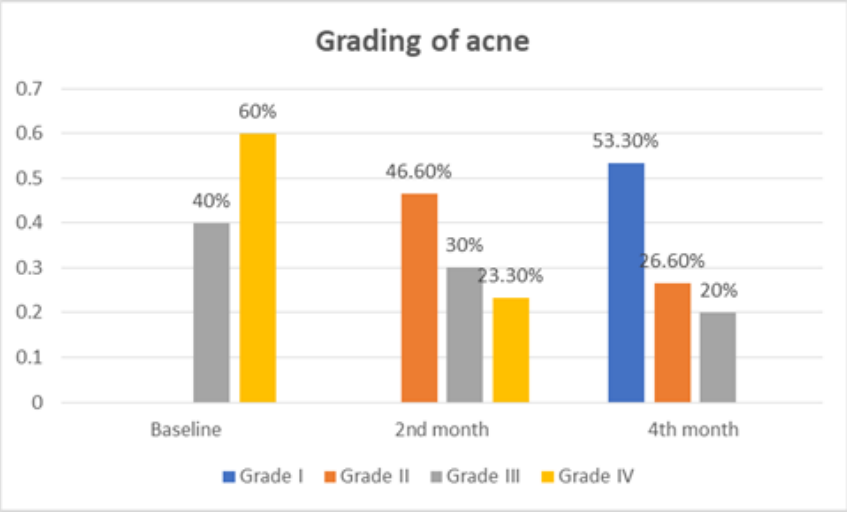


Lesion grading was assessed at baseline, as well as at the 2-month and 4-month follow-up visits. Both male and female participants showed a marked reduction in acne severity over the follow-up period.

Table 3: Grading of acne

Grade of acne	Baseline	2nd month	4th month
1	-	-	53.3%
2	-	46.6%	26.6%
3	40%	30%	20%
4	60%	23.3%	-

Graph 2: Grading of acne



First Visit

Figure 1:

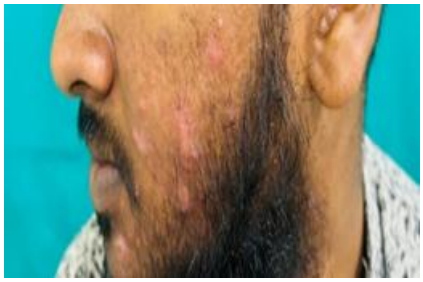
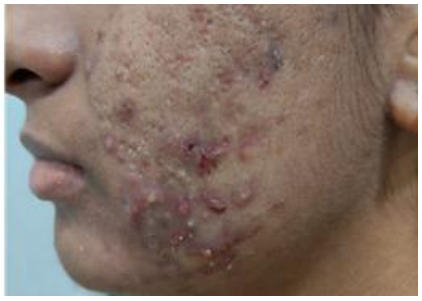


Figure 2:



After 4 Months of Isotretinoin

Figure 3:

Figure 4:

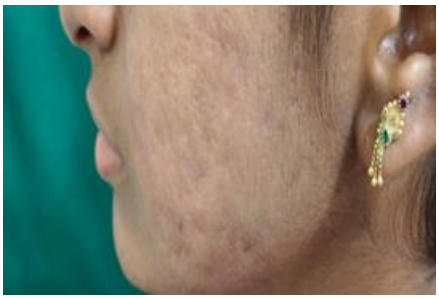
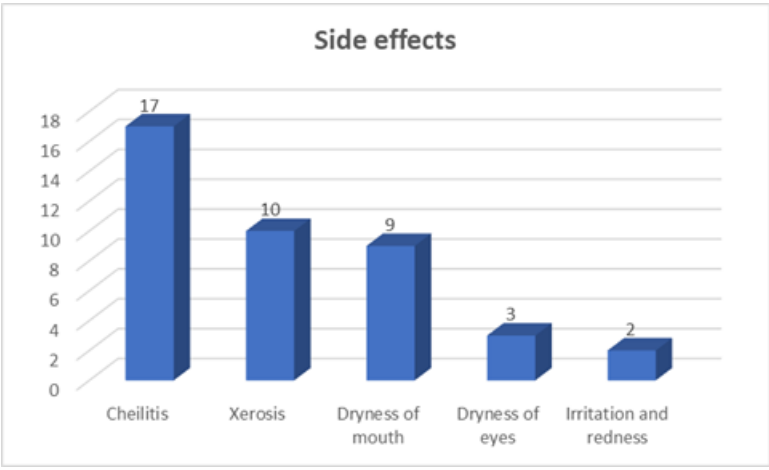


Table 4: Side effects seen in patients

Side effects	Number of participants	Percentage
Cheilitis	17	56.6%
Xerosis	10	33.3%
Dryness of mouth	9	30%
Dryness of eyes	3	10%
Irritation and redness	2	6.6%

Graph 3: Side effects



Among the adverse effects observed, cheilitis was the most frequently reported, affecting 17 participants (56.6%). This was followed by xerosis, noted in 10 individuals (33.3%), dryness of the mouth in 9 (30%),

dryness of the eyes in 3 (10%), and irritation with redness in 2 participants (6.6%).

The impact of isotretinoin on lipid profile was evaluated by measuring total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) levels. Liver function was assessed by monitoring aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels. These parameters were recorded at baseline, at the end of the second month, and at the fourth month of treatment.

Table 5: Summary of laboratory findings

	Baseline	**2 Months**	**4 Months**	**P-Value**
Total Cholesterol	137±12.5	163.3 ± 16.7	206.5±10.3	0.0001
Triglycerides	92.3±20.1	123.8 ± 13.9	153.2± 7.7	0.0001
LDL	89±8.8	96.3 ± 9.6	108.1± 14.4	0.0001
HDL	41.9±5.4	40.5 ± 2.9	34.6± 5.8	0.0001
AST	22.8±5.5	23.1 ± 5.4	23.2± 5.3	0.956
ALT	23.4±6.1	23.7 ± 6.2	23.8± 6.2	0.966

Lipid Profile and Liver Enzyme Changes during Isotretinoin Therapy

The study observed progressive increases in total cholesterol, triglycerides, and LDL cholesterol levels during isotretinoin therapy, while HDL cholesterol levels showed a consistent decline. These changes were statistically significant across all time points when compared with baseline values.

Total Cholesterol: At baseline, total cholesterol levels were 137 ± 12.5 mg/dL. At 2 months, levels increased to 163.3 ± 16.7 mg/dL and further increased to 206.5 ± 10.3 mg/dL by 4 months. These elevations were statistically significant ($P < 0.05$), indicating a notable impact of isotretinoin on total cholesterol levels.

Triglycerides: Baseline triglyceride levels measured 92.3 ± 20.1 mg/dL. Levels increased to 123.8 ± 13.9 mg/dL at 2 months and to 153.2 ± 7.7 mg/dL at 4 months. These changes were also statistically significant ($P < 0.05$), reflecting a significant treatment-associated rise in triglycerides.

LDL Cholesterol: LDL cholesterol levels increased from 89 ± 8.8 mg/dL at baseline to 96.3 ± 9.6 mg/dL at 2 months and 108.1 ± 14.4 mg/dL at 4 months. This upward trend was statistically significant ($P < 0.05$).

HDL Cholesterol: HDL levels showed a decreasing pattern, from 41.9 ± 5.4 mg/dL at baseline to 40.5 ± 2.9 mg/dL at 2 months and 34.6 ± 5.8 mg/dL at 4 months. The reduction in HDL was statistically significant ($P < 0.05$).

Liver Enzymes (AST and ALT): To evaluate the hepatic safety of isotretinoin, AST and ALT levels were measured. AST levels were 22.8 ± 5.5 U/L at baseline, 23.1 ± 5.4 U/L at 2 months, and 23.2 ± 5.3 U/L at 4 months. ALT levels were 23.4 ± 6.1 U/L at baseline, 23.7 ± 6.2 U/L at 2 months, and 23.8 ± 6.2 U/L at 4 months. Although both enzymes showed slight increases over time, these changes were within the normal range and did not reach statistical significance ($P > 0.05$). Isotretinoin therapy was associated with significant elevations in total cholesterol, triglycerides, and LDL cholesterol, along with a decrease in HDL cholesterol. However, liver function as indicated by AST and ALT levels remained stable and within normal limits,

suggesting no significant hepatotoxicity over the treatment period.

Discussion

Thirty Acne Vulgaris patients receiving oral isotretinoin treatment were included in this study; forty percent of the patients identified as male, and sixty percent identified as female. In their study on isotretinoin treatment for acne vulgaris, Ayush Jha et al[6] found a similar gender pattern, with a larger prevalence of female participants (n = 95; 63.33%) compared to male participants (n = 55; 36.66%). The average age of the male and female participants in this study was 23.8±3.4 and 22.47±3.2 years, respectively. These results are similar to those of Farzana Afroz et al[7], who found that the mean age of males was 22.0 ± 6.7 years, while the mean age of females was 24.0 ± 4.5 years.

Cheilitis was the most often reported adverse event in this trial, affecting 56.6% of individuals. In addition, xerosis was reported in 10 patients (33.3%), followed by oral dryness in 9 patients (30%), ocular dryness in 3 patients (10%), and redness and irritation of the eyes in 2 patients (6.6%).

In the study done by Dhir et al[8] mucocutaneous side effects and abnormal lipid profiles were seen. All (100%) patients showed evidence of cheilitis and dryness of lips was observed in 90% of the patients. Seven (14%) patients showed redness/dryness of the eyes.

In our study, all participants were administered low-dose oral isotretinoin at 0.2 mg/kg/day for a duration of four months. Conversely, Tan et al[9] reported using higher fixed doses ranging from 40 to 80 mg per day, with treatment durations varying between 3–6 months or as short as 3–6 weeks. Such variations may reflect differing physician approaches based on the severity of acne and individual patient characteristics. Furthermore, Tan et al[9] indicated that low-dose isotretinoin (10–20 mg/day) could be safely administered over longer periods (6–12 months), potentially resulting in fewer side effects.

The effects of isotretinoin medication on liver function and lipid profiles were examined in this study. Consistent after two months and at the end of treatment, the data demonstrated significant increases in total cholesterol, triglycerides, and LDL levels, as well as a significant decrease in HDL. These results align with the established dyslipidemia caused by isotretinoin, most likely as a result of its effect on hepatic lipid metabolism.

Although liver enzymes (AST and ALT) increased slightly, the changes were not statistically significant and remained within normal limits, indicating minimal hepatic impact in most patients.In our study, patients who received isotretinoin treatment had liver enzymes that were less altered than lipids.

Bhat R et al[10] conducted a prospective study involving 50 male and female participants with moderate to severe acne vulgaris. The subjects were administered oral isotretinoin at a dose of 20 mg/day (approximately 0.2–0.3 mg/kg/day) over a three-month period. Cheilitis was the most frequently reported side effect, observed in 98% of the participants. Other common adverse effects included xerosis (84%), dandruff (12%), facial erythema and rough, dry hair (8%), and dry mouth. The study also reported significant elevations in total cholesterol and serum triglyceride levels, with 6% of the patients showing values above the normal range. Additionally, liver enzyme levels increased significantly during the treatment, with 6% of participants exhibiting levels exceeding the normal limits.

Zane L et al,[11] conducted a study to determine the incidence of abnormal laboratory values in acne vulgaris patients on oral isotretinoin. Laboratory values of serum

TGs, TC, and liver transaminases were evaluated at the 2 months prior to initiation of oral Isotretinoin and after 3 months period. Substantial abnormalities in the lipids and liver transaminases were noted in > 79% compared with the baseline period.

In study by Ghalamkarpour et al, patients treated with 0-5mg/Kg/day reported statistically significant increase in triglyceride levels with no change in liver enzymes and cholesterol.[12] Mandal et al[13] found no significant changes in liver function tests following isotretinoin treatment.

Numerous studies in the literature have established that negative effects on lipid profiles and liver enzymes are reversible. Brito et al's study, on the other hand, reported no statistically significant changes in TG, HDL, LDL, or liver enzymes.[14]

Our results are in contrast to a research by Baxter et al. that included 30 patients and found no discernible changes in triglycerides, LDL, or HDL levels were measured at baseline and throughout isotretinoin treatment.[15]

Some research claims that individuals using isotretinoin need regular laboratory testing because of the substantial changes in their blood liver transaminase and lipid profile; other studies, however, conclude that these effects are mild and that no testing is necessary. [16]

Conclusion

This study demonstrates that oral isotretinoin therapy significantly reduces acne severity in young adults, with notable clinical improvement observed as early as the second month of treatment. The most common adverse effect was cheilitis, followed by xerosis and mucocutaneous dryness, all of which were manageable. Biochemical monitoring revealed a statistically significant rise in total cholesterol, triglycerides, and LDL cholesterol levels, accompanied by a significant decline in HDL cholesterol. Despite these lipid profile alterations, liver enzyme levels (AST and ALT) remained stable and within normal limits throughout the treatment duration, indicating preserved hepatic safety. These findings reinforce the therapeutic efficacy of isotretinoin in moderate to severe acne, while underscoring the importance of regular lipid monitoring during therapy.

List of abbreviations

TC-Total cholesterol

TG-Triglycerides

LDL- Low-density lipoprotein

HDL- High-density lipoprotein

AST- Aspartate aminotransferase

ALT-Alanine aminotransferase

Ethics approval: The study was approved by the institutional ethics committee.

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