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Dermatology

Isotretinoin's Impact on Liver Enzymes and Lipid profile in Acne Patients

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Abstract **Original Research Article**

***Background*:** Acne is a multifactorial skin lesion and a persistent inflammatory disorder of the pilosebaceous units. One of the most common skin problems, acne vulgaris, which predominantly affects teenagers but can affect anyone at any age, is treated by dermatologists. Objective: The goal of the current study was to assess the profile of changes in ALT, AST, and lipid profiles (TGs, LDL, and HDL) in these patients. ***Methodology*:** This cross-sectional study was conducted at tertiary care hospital Dhaka District from June 2020 to July 2022 in the Department of Dermatology. A total of 200 patients were participate in the study. Patients aged more than 15 years, both male and female and patients with diagnosed acne were included in the study. Severely ill patients and not willing to participate were excluded from the study. Data collection was done after approval of protocol using a semi-structured questionnaire through face to face interview. Data were analyzed using a computer programme SPSS 25.0 version. ***Result*:** The mean age of male was 22 (±6.7) while in case of female was 24 (±4.5). Minimum age of the patients was 18 year and maximum was 45 year. 75% of the respondents were female and 25% were male. The mean ((±SD)) RBC was 4.9 (0.5)×10^6 /mL, WBC was 8.4 (3.5)×10^3 /mL and Hb was 14.3 (1.7)×10^6 /mL, in case of female the Hb was 12.6 [1.5]× 10^6 /mL and 14.9 (1.1)×10^6 /mL for male. In this present study, we discovered that individuals who received isotretinoin medication was statistically significant increases in both TG and LDL levels. Additionally, we discovered statistically significant decreases in HDL levels. In our study, patients who received isotretinoin treatment had liver enzymes that were less altered than lipids. The clinical classification was unaffected, although there were statistically significant increases in AST levels. ALT levels raised as well, but the variations were not statistically significant. ***Conclusion*:** Although severe laboratory alterations were not noted in our study, we advise doctors to use caution when administering isotretinoin to patients with a history of abnormal findings. Overall, we advise dermatologists that isotretinoin can be administered with little concern regarding changes in serum transaminase and Lipid profile.

Keywords: Acne Vulgaris, Isotretinoin, Liver Enzyme, Lipid.

INTRODUCTION

The eighth most common illness in the world is acne vulgaris. 9.4% of people worldwide, according to estimates, suffer from acne vulgaris [1]. Between the ages of 11 and 30 years, around 80% of the population experiences breakouts of acne [2]. The majority (85%) of the population is affected with acne vulgaris, a chronic condition of the sebaceous glands. It is an inflammatory condition of the pilosebaceous units that manifests as seborrhea, papules, open and closed comedones, and in more severe cases, nodules, pseudocysts, and scarring [3]. Inflammatory and non-inflammatory acne are the two kinds of this disease, although they can coexist. As a result, the condition can be clinically divided into four levels: grade I, the mildest type of non-inflammatory acne, with comedones; grade II, inflammatory or papulopustular acne, in which papules and pustules are also present with comedones; grade III, nodulocystic acne; and grade IV, conglobate acne [4]. P. acnes, Staphylococcus epidermidis, and Malassezia furfur are the three main organisms obtained from the epidermis and pilosebaceous ducts of acne sufferers [5]. Depending on the severity of the acne, several topical medications, such as tretinoin, isotretinoin, adapalene, benzoyl

peroxide, and azelaic acid, can be used alone or in combination to treat non-inflammatory acne or moderate inflammatory acne [6]. Systemic treatment with antibiotics or isotretinoin may be used to treat more severe cases of acne. On the other hand, treatment should be based on the source of the excess androgen production when acne is caused by hyperandrogenism of adrenal or ovarian origin, such as in the case of polycystic ovary syndrome [7]. For the treatment of severe inflammatory acne of the nodulocystic or conglobate kinds as well as cases of acne that have shown resistance to prior antibiotic or topical treatment, the use of isotretinoin or 13-cis-retinoic acid is advised [8, 9]. In these situations, isotretinoin doses range from 0.5 mg/kg/day to 2 mg/kg/day for a duration of between 16 to 24 weeks. The medication should be administered up to a maximum cumulative dose of 120– 150 mg/kg. Additionally, numerous studies have demonstrated that for illness remission, the cumulative dose is more crucial than the daily amount [10, 11]. By interacting with particular retinoid receptors and altering gene transcription, isotretinoin possibly affects the sebaceous gland. After four weeks of treatment, the medicine reduces the gland's size and activity, which results in a reduction in the amount of sebum it generates. Additionally, retinoids like isotretinoin work by normalizing sebaceous follicle keratinization and the prevalence of *Propionibacterium acnes* [12]. There are many negative side effects associated with this medication. Teratogenicity is the most significant of them, but mucocutaneous effects like chapped lips, dry skin and nose, skin redness, eye irritation, and worsening of acne are the most prevalent [11]. Poor tolerance for contact lenses, increased S. aureus infection, and photophobia are some of the ocular-related side effects. Other less frequent adverse effects include weakness, weariness, hair loss, and headache. Use of isotretinoin may also result in changes to the liver, such as elevated serum levels of liver enzymes (liver aminotransferases) and lipids, such as elevated triglyceride, total cholesterol, and low-density lipoprotein (LDL) cholesterol levels and decreased high density lipoprotein (HDL) cholesterol levels [13-15]. Since oral isotretinoin is used to treat severe cases of acne, the goal of the current study was to assess the profile of changes in ALT, ASL, and lipids (TGs, LDL, and HDL) levels in these patients.

METHODOLOGY

This cross-sectional study was conducted at tertiary care hospital Dhaka District from June 2020 to July 2022 in the Department of Dermatology. A total of 200 patients were participate in the study. Patients aged from 18 to 45 years, both male and female and patients with diagnosed acne were included in the study. Severely ill patients and not willing to participate were excluded from the study. Aspartate aminotransferase and ALT levels were classified as normal (<40 U/L) and high (≥40 U/L). 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). Low-density lipoprotein levels were classified 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). High-density lipoprotein levels were classified as low (<40 mg/dL), normal (40–59 mg/dL), and high (≥60 mg/dL). Normal WBC was defined as 3.5 to 12.5×10^3 /mL. Normal hemoglobin count was defined as 11.5 to 15.0×10^6/mL for women and 13 to 17×10^6/mL for men. Normal RBC was defined as 4.0 to 5.2×10^6/mL for women and 4.5 to 5.9×10^6/mL for men. The detail of the study was explained to each eligible respondent and consent was taken. After collection, the data were checked and cleaned, followed by editing, compiling, coding and categorizing according to the objectives and variable to detect errors and to maintain consistency, relevancy and quality control. Data collection was done after approval of protocol using a semi-structured questionnaire through face to face interview, according to the objectives and variables by IBM software- Statistical package for Social Science (SPSS 25) version. In the case of variables with a normal distribution (parametric), Student's t-test was used to compare means between two groups and ANOVA for three or more groups. To compare proportions, Fisher's exact test was used. To establish correlations between variables, Spearman's correlation coefficient was calculated.

RESULTS

Table 1: Distribution of the respondents by mean age

Age	Male	Female
Mean (±SD)	22 (±6.7)	24 (±4.5)
Min-Max	18-45	

Table-1 shows the distribution of the respondents by mean age. The mean age of male was 22 (±6.7) while in case of female was 24 (±4.5). Minimum age of the patients was 18 year and maximum was 45 year.

Figure-1 shows 75% of the respondents were female and 25% were male.

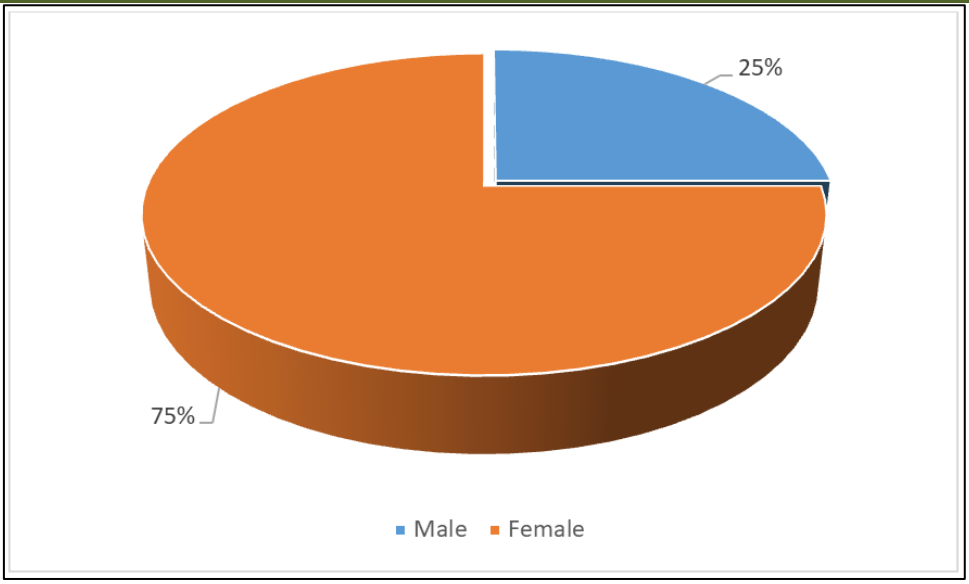

Figure 1: Distribution of the respondents by Sex

Table 2: Distribution of the respondents by blood profile

Blood profile	Mean (±SD)
RBC	4.9 (0.5)×10^6 /mL
WBC	8.4 (3.5)×10^3 /mL
Hb	14.3 (1.7)×10^6 /mL (women, 12.6 [1.5]× 10^6 /mL; men, 14.9 (1.1)×10^6 /mL).

Table-2 shows that the mean ((±SD)) RBC was 4.9 (0.5)×10^6 /mL, WBC was 8.4 (3.5)×10^3 /mL and Hb was 14.3 (1.7)×10^6 /mL, in case of female the Hb was 12.6 [1.5]× 10^6 /mL and 14.9 (1.1)×10^6 /mL for male.

Table 3: Distribution of the respondents by Effects of Oral Isotretinoin

Laboratory Value	Baseline N (%)	3 Months N (%)	6 Months N (%)	F Score, P Value
AST				
Normal (<40 U/L)	180 (90)	170 (85)	109 (54.5)	$F_{2,616}$□0.34, P□.54
High (≥40 U/L)	20 (10)	30 (15)	91 (45.5)	
ALT				
Normal (<40 U/L)	185 (92.5)	160 (80)	180 (90)	$F_{2,318}$□0.11, P□0.54
High (≥40 U/L)	15 (7.5)	40 (20)	20 (10)	
TG				
Normal (<150 mg/dL)	170 (85)	122 (61)	145 (72.5)	
Borderline high (150–199 mg/dL)	15 (7.5)	38 (19)	40 (20)	
High (200–499 mg/dL)	10 (5)	30 (15)	15 (15)	
Very high (≥500 mg/dL)	5 (2.5)	10 (5)	0 (0)	$F_{2,286}$□6.9, P□.001[b]
LDL				
Optimal (<100 mg/dL)	150 (75)	89 (44.5)	60 (30)	
Above optimal (100–129 mg/dL)	15 (7.5)	60 (30)	84 (42)	
Borderline high (130–159 mg/dL)	20 (10)	40 (20)	44 (22)	
High (160–189 mg/dL	10 (5)	7 (3.5)	8 (4)	$F_{2,382}$□51.2, P□.001[b]
Very high (≥190 mg/dL)	5 (2.5)	4 (2)	4 (2)	
HDL				
Low (<40 mg/dL)	50 (25)	60 (30)	47 (23.5)	
Normal (40–59 mg/dL)	150 (75)	120 (60)	117 (58.5)	
High (≥60 mg/dL)	50 (25)	20 (10)	36 (18)	$F_{2,384}$□5.2, P□.000[b]

AST(aspartate aminotransferase); ALT,(alanine aminotransferase), TG, (triglyceride); LDL, (low-density lipoprotein); HDL, (high-density lipoprotein). [b] Statistically significant.

Since the majority of patients received the same dosage, we hypothesized that differences between dosages and laboratory data would not be significantly different. Nearly all of the patients (95%) had normal AST and ALT levels at baseline. The results are outlined in the Table-3.

At baseline, normal AST levels in 180 (90%) patients and high in 20 (10%) patients. At 3-month follow-up normal AST levels in 170 (85%) patients and high levels in 30 (15%) patients. At 6-month follow-up, mean (SD) AST levels were 21.3 (5.7) U/L, with normal levels in 109 (54.5%) patients and high levels in 91 (45.5%) patients. Differences between AST levels at baseline and 3-month follow-up were not statistically significant (P=.4). Differences between AST levels at 3- and 6-month follow-up were not statistically significant (P=.5). Differences between AST levels at baseline and 6-month follow-up were statistically significant (P=.07). Differences between AST classifications at the 3 time points were not statistically significant ($F_{2,286}$ 6.9, P .001[b]). Overall, the results indicated that AST levels increased over time in patients treated with isotretinoin, but the increase was not above the normal range and was not statistically significant.

At baseline, ALT normal levels in 185 (92.5%) patients and high in 15 (7.5%) patients. At 3-month follow-up, ALT normal levels in 160 (80%) patients and high in 40 (20%) patients. At 6-month follow-up, normal ALT levels in 180 (90%) patients and high in 20 (10%) patients. Overall, ALT levels increased with time. Differences between ALT classifications at each time point were not statistically significant ($F_{2,318}$ 0.11, P 0.54). Overall, the results indicated that ALT levels increased over time in patients treated with isotretinoin, but the increase was not statistically significant.

Triglyceride levels were classified as normal, borderline high, high, and very high. Normal Triglyceride levels in 170 (85%) patients, borderline high in 15 (7.5%) patients, high in 10 (5%9) patients, and very high in 5 (2.5) patients. At 3-month follow-up, normal TG levels in 122 (61%) patients, borderline high in 38 (19%) patients, high in 30 (15%) patients, and very high in 10 (5%) patient. At 6-month follow-up, normal TG levels in 145 (72.5%) patients, borderline high in 40 (20%) patients, high in 15 (15%) patients, and very high in 0 (0%) patients. Differences between TG classifications at each time point were statistically significant ($F_{2,286}$ 6.7, P .001[b]). Overall, TG levels increased from baseline during isotretinoin treatment at 3- and 6-month follow-up, and these increases were above normal range; however, there was no statistically significant increase from 3- to 6-month follow-up.

Low-density lipoprotein levels were classified as optimal, above optimal, borderline high, high, and very high. At baseline, optimal LDL levels in 150 (75%) patients, above optimal in 15 (7.5%) patients, borderline high in 20 (10%) patients, high in 10 (5%) patients, and very high in 5 (2.5%) patients. At 3-month follow-up, optimal LDL levels in 89 (44.5%) patients, above optimal in 60 (30%) patients, borderline high in 40 (20%) patients, high in 7 (3.5%) patients, and very high in 4 (2%) patients. At 6-month follow-up, optimal LDL levels 60 (30%) patients, above optimal in 84 (42%) patients, borderline high in 44 (22%) patients, high in 8 (4%) patients, and very high in 4 (2%) patient. Differences between LDL classifications at each time point were statistically significant ($F_{2,382}$ 51.2, P .001[b]). Overall, statistically significant increases in LDL levels from baseline were noted during isotretinoin treatment and this increase was above normal range.

High-density lipoprotein levels were classified as low, normal, and high. At baseline, low level HDL in 50 (25%) patients, normal in 150 (75%) patients, and high in 50 (25%) patients. At 3-month follow-up, with low level HDL in 60 (30%) patients, normal in 120 (60%) patients, and high in 20 (10%) patients. At 6-month follow-up low level HDL in 47 (23.5%) patients, normal in 117 (58.5%) patients, and high in 36 (18%) patients. Differences between baseline HDL levels compared to 3-month follow-up were statistically significant (P=.001). Differences between baseline HDL levels compared to 6-month follow-up were statistically significant (P=.001). Differences in HDL levels at 3- and 6-month follow-up were statistically significant (P=.001). Differences between HDL classifications at each time point were statistically significant ($F_{2,384}$ 5.2, P .000[b]). Overall, there were statistically significant decreases in HDL levels during isotretinoin treatment from baseline and this decrease was above normal range; however, HDL levels did not decrease at 3- and 6-month follow-up.

DISCUSSION

This study was a cross-section observational study. The mean age of male was 22 (±6.7) while in case of female was 24 (±4.5). Minimum age of the patients was 18 year and maximum was 45 year. 75% of the respondents were female and 25% were male. The mean ((±SD)) RBC was 4.9 (0.5)×10^6 /mL, WBC was 8.4 (3.5)×10^3 /mL and Hb was 14.3 (1.7)×10^6 /mL, in case of female the Hb was 12.6 [1.5]× 10^6 /mL and 14.9 (1.1)×10^6 /mL for male.

Isotretinoin may change liver aminotransferases (AST and ALT), TGs, HDL, and LDL to varying degrees, according to studies investigating its effects on liver enzymes and lipids in the literature [6]. Between March 1995 and September 2002, 13,772 acne patients receiving oral isotretinoin therapy were investigated by Zane *et al.*, increased liver transaminase and serum Lipid profile were discovered by the researchers. They claimed that these anomalies

were typically reversible and temporary [15]. During isotretinoin medication, Bershad *et al.*, reported an increase in LDL and TG but a decrease in HDL. The lipid profile modifications also seemed to be temporary, returning to the baseline level two months after therapy ended [16].

No statistically significant changes in liver transaminase, TG, HDL, or LDL values were observed after isotretinoin treatment in one trial involving 150 patients, according to Brito *et al.*, [17]. Another study by Baxter *et al.*, observed no significant changes in TG, LDL, or HDL levels evaluated at baseline or throughout therapy with isotretinoin in a different research involving 30 patients [18]. Due to significant changes in blood liver transaminase and Lipid profile, some research contend that patients using isotretinoin require routine laboratory tests; however, other studies come to the opposite conclusion, finding that these effects are modest and no tests are required [19]. In this present study, we discovered that individuals who received isotretinoin medication saw statistically significant increases in both TG and LDL levels. Additionally, we discovered statistically significant decreases in HDL levels. In our study, patients who received isotretinoin treatment had liver enzymes that were less altered than lipids. The clinical classification was unaffected, although there were statistically significant increases in AST levels. ALT levels raised as well, but the variations were not statistically significant.

Limitations of the Study

The present study was conducted in a very short period due to time constraints and funding limitations. The small sample size was also a limitation of the present study.

CONCLUSION

Although severe laboratory alterations were not noted in our study, we advise doctors to use caution when administering isotretinoin to patients with a history of abnormal findings.

RECOMMENDATION

Overall, we advise dermatologists that isotretinoin can be administered with little concern regarding changes in serum transaminase and Lipid profile.

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DECLARATION

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Ethical Approval: The study was approved by the informed consent of the participant patients.

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