Dermatology Practical & Conceptual

Isotretinoin-Induced Hematuria in Acne Patients: Frequency, Risk Factors, and Management Recommendations from a Single-Center Study

Igor Kapetanović[1], Jelena Nojner[1], Ivan Soldatovic[2,4], Dubravka Zivanovic[1,4], Natasa Maksimovic[3,4], Milos Nikolic[1,4], Snezana Minic[1,4]

1 Clinic of Dermatology and Venereology, University Clinical Center of Serbia, Belgrade, Serbia
2 Institute of Medical Statistics and Informatics, Faculty of Medicine, University of Belgrade, Belgrade, Serbia
3 Institute of Epidemiology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia
4 University of Belgrade School of Medicine, Belgrade, Serbia

Key words: Isotretinoin, Hematuria, Acne, Adverse drug reaction, Renal safety

Citation: Kapetanović I, Nojner J, Soldatovic I, Zivanovic D, Maksimovic N, Nikolic M, Minic S. Isotretinoin-Induced Hematuria in Acne Patients: Frequency, Risk Factors, and Management Recommendations from a Single-Center Study. *Dermatol Pract Concept.* 2026;16(1):5768. DOI: https://doi.org/10.5826/dpc.1601a5768

Accepted: June 7, 2025; **Published:** January 2026

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

Corresponding Author: Igor Kapetanovic, Clinic of Dermatology and Venereology, University Clinical Center of Serbia, Pasterova 2, Belgrade, Serbia. ORCID: 0000-0003-4776-2312. E-mail: igor.kapetanovic@hotmail.com

ABSTRACT

Introduction: Isotretinoin-induced hematuria is very rare; it has been reported in one study and individual case reports but never proven statistically.

Objectives: To determine whether hematuria is statistically more significant in isotretinoin-treated acne patients than in non-isotretinoin-treated patients.

Methods: Cohort study of acne patients treated at the University Clinic of Dermatology between 01 September 2022 and 31 March 2024.

Results: Eight hundred and sixty-four acne patients were treated and reviewed; 69.3% (599/864) were treated with modalities other than isotretinoin, while 30.7% (265/864) were treated with isotretinoin. Of the isotretinoin patients, only 26% (69/265) had urinalysis done at least once during therapy. In the isotretinoin group, 13% (9/69) had at least one episode of hematuria during treatment, as did 2.9% (2/70) in the control group. Hematuria is significantly more frequent in the isotretinoin group compared to control (P=0.026), with a 5.1 (95% confidence interval (CI): 1.06–24.5) higher risk. Of the isotretinoin-induced hematuria patients, 66.6% were male. The mean duration of isotretinoin use for hematuria was 2.78 months. Comorbidities and minimal and maximal isotretinoin dosage were not correlated with hematuria.

Conclusion: Hematuria is significantly more frequent in patients on isotretinoin and is a side-effect of isotretinoin. In the majority of cases, isotretinoin should be continued. Patients should be stratified according to risk factors per guidelines for microhematuria and referred to urologists. Urinalysis should be a part of routine monitoring in patients on isotretinoin especially at the 2- and 4-month intervals.

Introduction

Acne vulgaris is a common chronic, multifactorial disease of pilosebaceous units that affects predominantly adolescents at least once in 70–85% of the population [1]. Studies have concluded that acne persists into the twenties in approximately 20–60% of individuals and results in permanent scarring in more than 20% of cases [2]. While topical medication and oral antibiotics are considered first line, systemic isotretinoin (13 cis-retinoic acid) is the first-line treatment of choice for moderate-to-severe acne unresponsive to conventional therapy [3,4]. Isotretinoin is a retinoid that acts through influencing cellular morphogenesis, epidermal turnover and growth, apoptosis, and differentiation by binding to specific parts of the gene promoter regions called retinoic acid response element (RARE) [5]. It also possesses indirect negative regulatory mechanisms with anti-proliferative and anti-inflammatory activities through downregulating non-RARE promoter genes [5].

Isotretinoin side effects are most commonly dose-dependent and seen on the skin and mucous membranes, but it also has systemic side effects on other systems such as the bones, muscles, central nervous system, eyes, ears, and gastrointestinal symptoms [6]. Isotretinoin side effects on the kidneys and urogenital system are very rare, with reports comprised mostly of a few studies and individual case reports/series [7]. Even more rare are episodes of gross or microscopic hematuria induced by isotretinoin. Hematuria is defined as an abnormal number of erythrocytes in the urine and is classified as gross (accompanied by a change in urine color) or microscopic (microhematuria) [8,9]. Microhematuria is a relatively common condition, with a reported prevalence of 6.5% in the normal population, with a range of 2.4–31.1%, depending on the study and population [10]. Five or more erythrocytes in the urine is deemed abnormal and pathological [8], but in some cases, per the 2020 American Urological Association (AUA) guidelines, microhematuria should be defined as ≥3 red blood cells per high-power field on microscopic evaluation of a single specimen [10]. As of July 2024, only four case reports [11-14] and one prospective study [8], for a total of 17 patients, have been reported as isotretinoin-induced hematuria in literature. The most comprehensive research on this topic to date was done by Yesilkaya et al., in which 88 subjects on isotretinoin (ages 16–32) and 52 subjects in the control group were monitored for six months; 17% (15/88) in the isotretinoin group had hematuria at least once, as did 7.7% subjects (4/52) in the control group. As hematuria and sex did not show a statistically significant correlation, the frequency rate was not considered different from that of the normal population (P=0.118) [8]. Thus, more studies are needed to test this hypothesis.

Objectives:

The objective of our study was to determine the frequency and possible predictors of hematuria, as well as other side effects, in acne patients during isotretinoin treatment and whether isotretinoin is a potential risk factor/statistically more likely to induce hematuria in comparison with a similar aged cohort of acne patients on non-isotretinoin therapy.

Methods

This study was approved by the Ethics Committee of University Clinical Center of Serbia, Belgrade, Serbia.

From our electronic medical records, we conducted a retrospective observational study and chart review and clinical data analysis of acne patients treated in the outpatient department at the Clinic of Dermatology and Venereology, University Clinical Center of Serbia during an 18-month period (01 September 2022–31 March 2024).

Patients were divided into two groups for analysis: those treated with isotretinoin versus those not treated with isotretinoin, receiving local, systemic antibiotics, spironolactone, or combination of therapeutic modalities (control group). Decision of therapeutic choice was based on clinical severity of acne and/or persistence despite first-line local and/or systemic therapy. Patients were assessed for eligibility based on the following criteria:

Inclusion criteria:

- Acne diagnosis
- Being treated with either isotretinoin or any other form of therapy
- Having one or more urine analysis done during the treatment period

Exclusion criteria:

- Pregnancy and/or lactation
- Liver function deficit
- Kidney function deficit
- Current or previous episodes of nephrolithiasis
- Personal history of urinary intervention or IgA nephropathy or similar nephropathies
- Use of drugs with common nephritic side effects
- Previous episodes of hematuria, whether idiopathic or secondary
- Positive family history of hematuria and/or kidney/urogenital disorders

A baseline analysis was performed for all patients on isotretinoin. Due to the retrospective nature of the study, the starting dose of isotretinoin varied among subjects. Special attention was paid to female patients not doing urinalysis during any noted menstruation in the records as well as a couple days afterwards.

The primary outcome was the presence of hematuria during acne therapy based on clinical documentation in medical records. The presence of five or more erythrocytes in one or more urinalysis samples during therapy was considered pathological.

Results are presented as count (%), means ± standard deviation (SD) or median (25^{th}–75^{th} percentile) depending on data type and distribution. Groups were compared using parametric (t-test) and nonparametric (chi-square, Fisher's exact test and Mann-Whitney U test) tests. Logistic regression was performed to evaluate the relationship between dependent variables and independent variables. All p-values less than 0.05 were considered significant. All data were analyzed using SPSS 29.0 and R 3.4.2.

Results

During this time frame, 864 patients with a diagnosis of acne were treated: 69.3% (599/864) were treated with modalities other than isotretinoin, while 30.7% (265/864) were treated with isotretinoin. Of the isotretinoin patients, only 26% (69/265) had urinalysis done at least once during therapy. In the control group, 11.7% (70/599) had urinalysis in their records while on non-isotretinoin acne therapy.

A total of 139 patients were analyzed: 69 on isotretinoin therapy and 70 in the control group. In the isotretinoin group, the average age was 18.8±3.6 (range 13–30 years) versus 18.6±5.1 (range 12–42 years) in the control group. Patient characteristics are presented in Table 1. While no statistical difference in age was noted, the female sex was dominant in the control group. Males constituted 52.2% of the isotretinoin group but only 35.7% in the control group (P=0.051). This suggests males make up a larger portion of patients that have severe acne requiring isotretinoin treatment. The mean weight was 66.7±14.8 kg in the isotretinoin cohort, while the mean minimum and maximum dose of isotretinoin were 0.45±0.12 mg/kg and 0.69±0.21 mg/kg, respectively. Sex distribution and mean age were not significantly different between groups. Due to the retrospective nature of the study and often different providers giving treatment, urinalysis was done in the isotretinoin group in 73.9% of patients within the first two months, in 52.2% of patients between 3–5 months, and in only 15.9% after six months or more of isotretinoin use. The control group more frequently used other drugs like antibiotics and local creams. The isotretinoin group had significantly more comorbidities compared to controls and more frequently had patients with increased transaminases (14.5% vs. 4.3%; P=0.039) and hyperlipidemia (29.0% vs 4.3%; P<0.001).

In the isotretinoin group, nine patients (13%) experienced at least one episode of hematuria during treatment, compared to two patients (2.9%) in the control group. Hematuria was significantly more frequent in the isotretinoin group, compared to control (P=0.026). Furthermore, patients on isotretinoin had a 5.1 (95% CI: 1.06–24.5) higher risk of having hematuria compared to the control group. In the isotretinoin group, six of the subjects who had hematuria were male (66.6%) and three (33.3%) were female; in the control group, both subjects with hematuria were female. The mean duration of isotretinoin use when complete urinalysis first showed hematuria was 2.78 months, with 66.7% (6/9) having hematuria appear for the first time within the first two months of isotretinoin use; 33.3% (3/9) had hematuria at the 4-month mark of use, while 22.2% (2/9) were positive at the 6-month mark.

The distribution of patients in terms of adverse events and their correlation with hematuria is presented in Table 2. Approximately one quarter of the patients on isotretinoin had self-reported adverse events (including hair loss, cheilitis, xerosis, cramps, epistaxis, increased transaminases, and so on), the majority were local in nature, and the most frequent were cheilitis and xerosis. No significant difference was observed between patients with and without hematuria regarding the presence of adverse events (Table 2); however, the small number of patients in the hematuria-positive subgroup is a limiting factor in this analysis.

Factors and potential predictors associated with hematuria patients on isotretinoin are shown in Table 3. The average age of patients with hematuria is lower compared to patients without hematuria (16.8±2.7 vs. 19.1±3.7; P=0.067). The percentage of patients with hematuria was higher in males, but no significance was observed (P=0.481). The duration of acne before therapy as well as the duration of isotretinoin use was similar in both groups of patients, i.e., those with

Table 1. Isotretinoin and control group characteristics.

	Isotretinoin		p-value
	Yes (N=69)	No (N=70)	
Age (yrs.)	18.8±3.6	18.6±5.1	0.736 [a]
Sex male	36 (52.2%)	25 (35.7%)	0.051 [b]
Weight (kg)	66.7±14.8		
Duration of			
Acne before therapy	3 (2.5)		
Isotretinoin	6.1±2.7		
Isotretinoin dose			
Min	0.45±0.12		
Max	0.69±0.21		
Isotretinoin duration when urine was taken* (months)			
1-2	51 (73.9%)		
3-5	36 (52.2%)		
6+	11 (15.9%)		
Isotretinoin cumulative dose	99.4±47.7		
Hematuria	9 (13%)	2 (2.9%)	0.026 [b]
Drugs [‡]	22 (31.9%)	70 (100%)	<0.001[b]
Prednisone	8 (11.6%)	0	0.003 [c]
Spironolactone	6 (8.7%)	7 (10%)	0.792 [b]
Antibiotics	15 (21.7%)	33 (47.1%)	0.002 [b]
Local	1 (1.4%)	67 (95.7%)	<0.001 [b]
OCT	2 (2.9%)	0	0.245 [c]
Comorbidities	5 (7.2%)	0	0.028 [c]
Transaminase increase	10 (14.5%)	3 (4.3%)	0.039 [a]
Hyperlipidemia	20 (29.0%)	3 (4.3%)	<0.001 [b]
Increase of CK	3 (4.3%)	0	0.120 [c]

*Categories are independent and cannot be summed to 100%; [a]t test [b]Peason chi-square test [c]Fisher's exact test.

[‡]Percentages for individual drugs do not sum to 100% because patients could receive more than one type of medication. The overall number of patients receiving any additional treatment was 22 (31.9%) out of 69. Abbreviations: OCT: oral contraceptives; CK: creatine kinase.

Table 2. Adverse events in correlation with hematuria in patients on isotretinoin therapy.

	Total	Hematuria		p-value
	(N=69)	No (N=60)	Yes (N=9)	
Adverse events	19 (27.5%)	18 (30%)	1 (11.1%)	0.427 [c]
Local	16 (23.2%)	15 (25%)	1 (11.1%)	
Systemic	2 (2.9%)	2 (3.3%)	0	
Local + systemic	1 (1.4%)	1 (1.6%)	0	
Hair loss	1 (1.4%)	1 (1.6%)	0	1.000 [c]
Cheilitis	9 (13%)	9 (15%)	0	0.594 [c]
Xerosis	6 (8.7%)	5 (8.3%)	1 (11.1%)	0.582 [c]
Cramps	1 (1.4%)	1 (1.6%)	0	1.000 [c]
Epistaxis	1 (1.4%)	1 (1.6%)	0	1.000 [c]
Transaminase elevation	3 (4.3%)	3 (5%)	0	1.000 [c]

[c]Fisher's exact test.

Table 3. Factors associated with hematuria in patients on isotretinoin.

	Hematuria		p-value
	No (N=60)	Yes (N=9)	
Age (years)	19.1±3.7	16.8±2.7	0.067 [a]
Sex			
Male	30 (83.3%)	6 (16.7%)	0.481 [c]
Female	30 (90.9%)	3 (9.1%)	
Weight (kg)	66.2±13.8	70.0±20.9	0.473 [a]
Duration of (months)			
Acne before therapy	3 (2.0)	3 (3.3)	0.977 [d]
Isotretinoin	6.12±2.84	6.11±2.04	
Isotretinoin dosage			
Min	0.44±0.12	0.47±0.09	0.454 [a]
Max	0.69±0.21	0.66±0.21	0.594 [a]
Isotretinoin cumulative dose	100.4±50.5		
Comorbidities			
No	55 (85.9%)	9 (14.1%)	1.000 [c]
Yes	5 (100%)	0 (0%)	
Transaminase increase			
No	51 (86.4%)	8 (13.6%)	1.000 [c]
Yes	9 (90%)	1 (10%)	
Hyperlipidemia			
No	44 (89.8%)	5 (10.2%)	0.431 [c]
Yes	16 (80%)	4 (20%)	
Increase of CK			
No	57 (86.4%)	9 (13.6%)	1.000 [c]
Yes	3 (100%)	0 (0%)	

[a]t-test [b]Peason chi-square test [c]Fisher's exact test [d]Mann-Whitney U test. Abbreviation: CK: creatine kinase.

and those without hematuria. Comorbidities, minimal and maximal isotretinoin dosages, and increased liver transaminases were not correlated with hematuria. Patients with hyperlipidemia had two times higher percentage of hematuria compared to patients with normal lipid status, but no significance was observed.

The distribution of patients on isotretinoin and other drugs related to hematuria are presented in Table 4. As shown in the table, no significant association with other drugs was observed, but the patients on antibiotics had a higher percentage of hematuria (26.7% vs 9.3%).

Discussion

While isotretinoin is the most effective method of treatment and generally well tolerated, it causes many side effects in any organs that possess retinoic acid receptors [15]; however, little is known of its effects on the kidneys and genitourinary tract. In a recent review on this topic by Forouzani et al., only five case reports and six experimental studies were included [7]. According to literature, the first reported case to be found was of a 34-year-old male with microscopic hematuria and proteinuria on 40 mg/day isotretinoin after two months, but he also had a history of pelvic fracture six months previously, which could be a possible explanation and cause [11]. The second reported case involved a 16-year-old male patient receiving isotretinoin at 0.5 mg/kg/day. After one month of treatment, hematuria was observed, and secondary xerosis of urinary tract mucosa was proposed as the underlying mechanism. This theory was introduced for the first time in the literature [12]. To the best of our knowledge, other therapeutic options (antibiotics, spironolactone, and so on) have not been reported to be associated with hematuria in acne patients. In the most recent case, a 16-year-old male patient had isotretinoin-induced hematuria after two months of 0.6 mg/kg isotretinoin therapy with multiple episodes of hematuria after subsequent challenge and dechallenges [14]. Isotretinoin was continued in all the patients included in our study that had hematuria (for some patients, isotretinoin was never discontinued or only for a 1–2 week

Table 4. Drugs in correlation with hematuria in patients on isotretinoin.

	Hematuria		p-value
	No (N=60)	Yes (N=9)	
Drugs			
No	42 (89.4%)	5 (10.6%)	0.452 [c]
Yes	18 (81.8%)	4 (18.2%)	
Prednisone			
No	52 (85.2%)	9 (14.8%)	0.584 [c]
Yes	8 (100%)	0 (0%)	
Spironolactone			
No	54 (85.7%)	9 (14.3%)	1.000 [c]
Yes	6 (100%)	0 (0%)	
Antibiotics			
No	49 (90.7%)	5 (9.3%)	0.095 [c]
Yes	11 (73.3%)	4 (26.7%)	
Local			
No	59 (86.8%)	9 (13.2%)	1.000 [c]
Yes	1 (100%)	0 (0%)	
OCT			
No	58 (86.6%)	9 (13.4%)	1.000 [c]
Yes	2 (100%)	0 (0%)	

[c]Fisher's exact test. Abbreviation: OCT: oral contraceptives.

pause while awaiting results) as additional evaluations were for the most part within normal limits. Our observations and experience with isotretinoin-induced hematuria showed that when isotretinoin dosage was decreased immediately or either discontinued for 1–2 weeks followed by continuation with a lower dose, urinalysis was always within normal limits at follow-up. This implies a causality but not quite a dose dependence correlation in nature, despite the fact that our analysis (minimal dose P=0.454, maximum dose P=0.594) did not find a statistically significant correlation regarding dosage, similar to Yesilkaya et al. [8]. This also aligns with the theory that the half-life of isotretinoin and its metabolites is roughly 24 hours and thus takes nearly one week to be eliminated from the body [11]. This is the first study to conclude with statistical significance that isotretinoin is a risk factor and induces hematuria. It could potentially be speculated that additional renal or genitourinary effects of isotretinoin may be underreported.

For microscopic hematuria, no underlying etiology was found in roughly 40% of published reports [16]. Isotretinoin is often not thought of or regarded as a possible cause despite certain data pointing to a larger-than-expected prevalence [8]. If hematuria occurs at the end of a urine stream, it may have a prostatic, bladder, or trigonal causes and thus requires workup [17]. Physicians should also know about and thus question patients about certain ingested substances (rifampin, rhubarb, blueberries, fava beans) that can change the color of the urine and which can be inaccurately mistaken for blood, leading to potentially expensive and invasive therapeutic diagnostics [18]. Published reports indicate that infection accounts for 25% of hematuria cases and nephrolithiasis another 20% [19].

Newer monitoring acne management recommendations and guidelines rarely [4,20], if ever, mention performing urinalysis; in the clinical setting of our study, only 26% of isotretinoin patients had at least one urinalysis done. Our study showed that over half of hematuria patients will have pathological results within the first two months, and the vast majority within four months.

In terms of other adverse events, our results for the most part fall in line with other major studies. Liver dysfunction and altered transaminases has been reported to be 7.2% (all grade 1) in 704 patients [21], while ours was twice as much, with 14.5% (10/69), also all grade 1. In a retrospective cohort study of 13,772 patients on isotretinoin, the cumulative incidence of new abnormalities in patients with normal baseline values was 44% for triglycerides and 31% for cholesterol [22], while in our study it was lower, with 29% overall (20/69). In terms of creatinine kinase (CK), Landau et al. revealed CK elevations are frequently asymptomatic, and out of 442 patients, seen at least once in 37.3% of

patients [23]; in our study, 4.3% patients had elevated CK. Finally, leukopenia was reported in 8.2% patients on isotretinoin in a study [21], whereas none had it in our cohort. In general, the consensus is that these events are transient and reversible, as seen in our study as well.

There are no specific guidelines regarding diagnostics and evaluation for isotretinoin-induced hematuria. In general terms of hematuria, there are multiple factors to consider. Regarding prognosis and diagnostics, as per the AUA risk strata (low, intermediate, and high risk) based on age, sex, degree and persistence of microhematuria, and smoking, a study by Woldu et al. included 15,779 patients, of whom 4.6% were low risk, 11.8% intermediate, and the rest were high risk. Overall, 5.4% were diagnosed with bladder cancer (more prevalent in males, smokers, and older patients) [24]. This emphasizes the value of early identification of hematuria to prevent more serious renal or urothelial complications. Furthermore, the incidence of cancer in the low-risk group was 0.4% (3/727) and 1.0% in the intermediate group (18/1863) [24]. The 2020 AUA guidelines for asymptomatic microhematuria recommends history and focused exam for risk factors for urothelial cancer and non-malignant cancer, then cystoscopy and CT urogram if high risk, cystoscopy and renal ultrasound if intermediate risk and shared decision-making to either repeat urinalysis within six months or evaluate with cystoscopy and renal ultrasound [10]. Finally, there is the question of how often patients with microhematuria are referred to urologists. In a published report, only 1.7% (7,778/456,674) of microhematuria patients were seen by urologists [25,26]. With all these facts in mind, we must consider the fact that the vast majority of isotretinoin-induced hematuria patients are healthy, younger adults, predominately male, who would be classified as low risk, along with the low risk of bladder cancer. Recommendation can be hypothesized and suggested: In young, healthy, low-risk patients on isotretinoin with only microhematuria and no other symptoms or pertinent history, isotretinoin can be continued, preferably with a decreased dose and referral to an urologist for further evaluation and optional diagnostics per joint decision.

In patients with ≥3 RBC on isotretinoin if they do not have all of the following to be classified as low risk (i)faemale age <50, male age <40; ii) never smoked or <10 pack years; iii) no additional risk factor for urothelial cancer; iv) no prior episode of microhematuria), then isotretinoin should be discontinued and the patient referred to a urologist for further workup (renal ultrasound and cystoscopy as per AUA guidelines. If the patient is low risk, then clinical judgement should be made on a case-by-case basis whether to potentially decrease the isotretinoin dosage. Finally, this study potentially emphasizes the importance of counseling and informing patients about the potential hematuria risk while taking isotretinoin.

Overall, a limitation of this study is due to its retrospective, single-center design and overreliance of medical notes and lack of an overall homogenous protocol for acne therapy. In general, while a much higher number of patients were not treated with isotretinoin, only a small number of patients had urinalysis done while being treated because urinalysis is not indicated while on topical and/or antibiotic therapy. Prospective studies with larger cohorts are needed that will potentially reach statistical significance with regards to potential predictive factors and associated patient characteristics that our study was not able to achieve.

Conclusion

In conclusion, acne patients on isotretinoin have a 5.1 (95% CI: 1.06–24.5) higher risk of having hematuria than do acne patients treated with other modalities in the control group. Hematuria is significantly more frequent in patients on isotretinoin compared to controls (P=0.026). Male subjects were affected more in terms of hematuria, but this was not statistically significant. In the majority of cases, isotretinoin should be continued. Detailed anamnesis should be taken, and patients should be stratified according to risk factors as per guidelines for microhematuria and referred to urologists. Urinalysis should be a part of routine follow-up monitoring in patients on isotretinoin, especially at the 2- and 4-month intervals. Potential specific predictors (age, weight, duration of acne, duration of isotretinoin use, isotretinoin doses, et cetera) and correlations were not found as no significant difference was observed between patients with and without hematuria regarding the presence of adverse events. This is most likely due to a very small number of patients in the hematuria positive subgroup, which is a limiting factor in this analysis. We hope our study will raise awareness among dermatologists, urologists and general practitioners of this association. We also hope this study will motivate further prospective studies with larger patient cohorts so as to be able to determine predictors and associated correlations while also giving answers to the mechanism of action of isotretinoin induced hematuria.

Abbreviations: AUA: American Urological Association; CK: creatine kinase; RARE: retinoic acid response element.

References

1. Dreno B, Poli F. Epidemiology of acne. *Dermatology.* 2003;206(1):7–10. DOI: 10.1159/000067817. PMID: 12566799.

2. Kutlu Ö, Karadağ AS, Wollina U. Adult acne versus adolescent acne: a narrative review with a focus on epidemiology to treatment. *An Bras Dermatol*. 2023;98(1):75–83. DOI: 10.1016/j
3. .abd.2022.01.006. PMID: 36253244.
4. Thielitz A, Krautheim A, Gollnick H. Update in retinoid therapy of acne. *Dermatol Ther.* 2006;19(5):272–279. DOI: 10.1111/j .1529-8019.2006.00084.x. PMID: 17014482.
5. Santer M, Burden-Teh E, Ravenscroft J. Managing acne vulgaris: an update. *Drug Ther Bul.l* 2023;62(1):6–10. DOI: 10.1136 /dtb.2023.000051. PMID: 38154809
6. Nelson AM, Zhao W, Gilliland KL, Zaenglein AL, Liu W, Thiboutot DM. Isotretinoin temporally regulates distinct sets of genes in patient skin. *J Invest Dermatol*. 2009;129(4):1038–1042. DOI: 10.1038/jid.2008.338. PMID: 18987667.
7. Ahmad HM. Analysis of clinical efficacy, side effects, and laboratory changes among patients with acne vulgaris receiving single versus twice daily dose of oral isotretinoin. *Dermatol Ther.* 2015;28(3):151–157. DOI: 10.1111/dth.12213. PMID: 25754162.
8. Forouzani-Haghighi B, Karimzadeh I. Isotretinoin and the Kidney: Opportunities and Threats. *Clin Cosmet Investig Dermatol*. 2020;13:485–494. DOI: 10.2147/CCID.S259048. PMID: 32801824
9. Yesilkaya B, Alli N, Artuz RF, Ulu E, Kartal D, Cinar SL. The frequency of hematuria in acne vulgaris patients during isotretinoin treatment. *Cutan Ocul Toxicol*. 2017;36(1):74–76. DOI: 10.3109/15569527.2016.1155595. PMID: 26938860.
10. Grossfeld GD, Litwin MS, Wolf JS et al. Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy--part I: definition, detection, prevalence, and etiology. *Urology.* 2001;57(4):599–603. DOI: 10.1016/s0090-4295(01)00919-0. PMID: 11306356.
11. Barocas DA, Boorjian SA, Alvarez RD et al. Microhematuria: AUA/SUFU Guideline. *J Urol*. 2020;204(4):778-786. DOI: 10.1097/JU.0000000000001297. PMID: 32698717.
12. Pavese P, Kuentz F, Belleville C, Rougé PE, Elsener M. Renal impairment induced by isotretinoin. *Nephrol Dial Transplant*. 1997;12(6):1299. DOI: 10.1093/ndt/12.6.1299a. PMID: 9198075.
13. Sarifakioglu E, Yilmaz AE, Erpolat S. Terminal hematuria associated with oral isotretinoin treatment in a patient with acne vulgaris. *Pediatr Dermatol.* 2012;29(5):668–669. DOI: 10.1111/j.1525 -1470.2011.01552.x. PMID: 22067016.
14. Erdik A, Cimen HI, Atik YT, Gul D, Pinar M. *New J Urol*. 2023;18(2):183-185. DOI : 10.33719/yud.2023;18-2-1210144.
15. Kapetanovic I, Zivanovic D, Mijuskovic M, Minic S. The unknown silent drug reaction in acne patients: rare case of isotretinoin-induced haematuria. *Fam Pract*. 2024;41(4):615-617. DOI: 10.1093 /fampra/cmad043. PMID: 37602648.
16. McLane J. Analysis of common side effects of isotretinoin. *J Am Acad Dermatol.* 2001;45(5):S188-194. DOI: 10.1067 /mjd.2001.113719. PMID: 11606952.
17. Khadra MH, Pickard RS, Charlton M, Powell PH, Neal DE. A prospective analysis of 1,930 patients with hematuria to evaluate current diagnostic practice. *J Urol*. 2000;163(2):524–527. DOI: 10.1016/S0022-5347(05)67916-5. PMID: 10647670.
18. Grossfeld GD, Carroll PR. Evaluation of asymptomatic microscopic hematuria. *Urol Clin North Am*. 1998;25(4):661–676. DOI: 10.1016/s0094-0143(05)70055-0. PMID: 10026773.
19. Sokolosky MC. Hematuria. *Emerg Med Clin North Am*. 2001;19(3):621–632. DOI: 10.1016/s0733-8627(05)70206-6. PMID: 11554278.
20. Quigley R. Evaluation of hematuria and proteinuria: how should a pediatrician proceed? *Curr Opin Pediatr.* 2008;20(2):140–144. DOI: 10.1097/MOP.0b013e3282f55f6c. PMID: 18332708.
21. Fallah H, Rademaker M. Isotretinoin for acne vulgaris - an update on adverse effects and laboratory monitoring. *J Dermatolog Treat*. 2022;33(5):2414–2424. DOI: 10.1080/09546634.2021.1967269. PMID: 34379039.
22. Öktem A, Hayran Y, Arı E, Yalçın B. Minimize the regular laboratory monitoring during the systemic isotretinoin treatment: data of 704 patients with acne vulgaris. *J Dermatolog Treat*. 2019;30(8):813–817. DOI: 10.1080/09546634.2019.1591578. PMID: 30836808.
23. Zane LT, Leyden WA, Marqueling AL, Manos MM. A population-based analysis of laboratory abnormalities during isotretinoin therapy for acne vulgaris. *Arch Dermatol*. 2006;142(8):1016–1022. DOI: 10.1001/archderm.142.8.1016. PMID: 16924051.
24. Landau M, Mesterman R, Ophir J et al. Clinical significance of markedly elevated serum creatine kinase levels in patients with acne on isotretinoin. *Acta Dermato-Venereologica*. 2001;81(5):350–352. DOI: 10.1080/000155501317140070. PMID: 11800143.
25. Woldu SL, Ng CK, Loo RK et al. Evaluation of the New American Urological Association Guidelines Risk Classification for Hematuria. *J Urol*. 2021;205(5):1387–1393. DOI: 10.1097 /JU.0000000000001550. PMID: 33356483.
26. Loo RK, Lieberman SF, Slezak JM et al. Stratifying risk of urinary tract malignant tumors in patients with asymptomatic microscopic hematuria. *Mayo Clin Proc*. 2013;88(2):129–138. DOI: 10.1016/j.mayocp.2012.10.004. PMID: 23312369.
27. Ghandour R, Freifeld Y, Singla N, Lotan Y. Evaluation of Hematuria in a Large Public Health Care System. *Bladder Cancer.* 2019;5(2):119–129. DOI: 10.3233/BLC-190221. PMID: 31930164.