Türk Klinik Biyokimya Derg 2025; 23(3): 139-142

https://doi.org/10.56615/tkbd.2025.17

Olgu Sunumu / *Case Report*

A Case of Unexpected Elevated Bilirubin Levels in Urine

İdrarda Beklenmeyen Bilirubin Yüksekliği Vakası

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Received / Başvuru Tarihi: 04.08.2025 *Accepted* / Kabul Tarihi: 25.09.2025

ABSTRACT

Complete urinalysis is commonly requested by clinicians, because it provides important information about diabetes, liver or urinary system diseases, hydration, urinary tract infections and many other clinical conditions. The results of complete urinalysis can be influenced by various factors, such as diet, dietary supplements and medications. In this case report, a false-positive urine bilirubin result caused by taking an anti-inflammatory drug containing etodolac was presented.

Keywords: Bilirubin, Etodolac, Interference, Complete urinalysis.

ÖZET

Tam idrar analizi diyabet, karaciğer veya üriner sistem hastalıkları, hidrasyon, idrar yolu enfeksiyonları ve birçok klinik durum hakkında önemli bilgiler sağladığı için klinisyenler tarafından sıklıkla istenir. Tam idrar analizi sonuçları diyet, gıda takviyeleri ve ilaç tedavileri dahil olmak üzere birçok faktörden etkilenebilir. Bu vaka sunumunda idrarda etodolak etken maddeli antienflamatuvar bir ilaç alımı kaynaklı yanlış pozitif idrar bilirubin vakası sunuldu.

Anahtar sözcükler: Bilirubin, Etodolak, İnterferans, Tam idrar analizi.

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Etik onay: Hastadan bilgilendirilmiş onam formu alınmıştır

INTRODUCTION

Complete urinalysis is a non-invasive, rapid, and cost-effective diagnostic tool in clinical practice (1). It is widely used for the diagnosis and clinical monitoring of various systemic and urinary disorders. Under normal physiological conditions, bilirubin is absent in urine. Its presence is always considered pathological and may indicate an underlying hepatobiliary disorder.

Dipstick tests used for urinalysis may yield false-positive or false-negative results in urinary bilirubin detection (2). Inaccurate urinalysis results are often caused by pre-analytical errors such as improper storage conditions, delayed transport, or interference from certain medications and their metabolites (3). Several drugs that interfere with urinary bilirubin testing have been reported in the literature (4). In this case report, we present a patient with a false-positive urinary bilirubin test result associated with the use of a nonsteroidal anti-inflammatory drug containing etodolac.

CASE PRESENTATION

A 60-year-old male patient was referred to our laboratory during routine check-ups because of +3 urinary bilirubin positivity, despite a serum total bilirubin level of 0.43 mg/dL and a direct bilirubin level of 0.20 mg/dL. The patient had no known comorbidities or abnormal physical examination findings apart from hypothyroidism, hyperlipidemia, and benign prostatic hypertrophy. The patient's clinical chemistry and complete urinalysis test results are presented in Table 1.

Complete urinalysis was performed using both the DIRUI FUS-200 and DIRUI FUS-2000 urine analyzers (DIRUI Industrial Co., China). No pathological findings were detected other than +3 bilirubin positivity, and further investigation was initially deemed unnecessary based on the remaining medical laboratory test results. In addition, the physical characteristics of the urine did not support the presence of bilirubinuria (Figure 1).

To rule out pre-analytical and analytical errors, a fresh spot urine sample was requested from the patient on the same day. In this sample, bilirubin was detected as +2 positive using both the DIRUI FUS-200 and DIRUI FUS-2000 urine analyzers, as well as by manual urine dipstick testing. Due to suspicion of a false-positive urinary bilirubin result, the patient was asked whether he was using any herbal products, dietary supplements, or medications. The patient reported the use of a nonsteroidal anti-inflammatory drug containing etodolac. Furthermore, review of the assay kit package insert revealed that etodolac metabolites may interfere with urinary bilirubin testing and potentially lead to false-positive results.

Figure 1. The patient's urine specimen collected in the etodolac treatment period

Şekil 1. Etodolak tedavisi döneminde toplanan hastaya ait idrar örneği

Table 1. Clinical chemistry and complete urinalysis test results of the patient
Tablo 1. Hastanın klinik kimya ve tam idrar tahlili test sonuçları

Parameters	Results	Reference Values
Glucose, mg/dL	101	70-110
Urea, mg/dL	15.50	6-20
Creatinine, mg/dL	0.85	0.7-1.2
AST, U/L	15	0-37
ALT, U/L	13	0-41
ALP, U/L	109	0-129
GGT, U/L	19	10-71
Total bilirubin, mg/dL	0.43	0-1.1
Direct bilirubin, mg/dL	0.20	0-0.3
Indirect bilirubin, mg/dL	0.23	0-0.8
Na^+, mEq/L	140	135-145
K^+, mEq/L	4.90	3.5-5.1
Cl^-, mEq/L	101	98-107
Complete urinalysis		
Color	Light yellow	Light yellow
Clarity	Clear	Clear
Specific gravity	1018	1015-1025
pH	6	5.0-8.5
Glucose	Negative	Negative
Protein	Negative	Negative
Ketone	Negative	Negative
Bilirubin	+3	Negative
Urobilinogen	Normal	Normal
Nitrite	Negative	Negative
Ascorbic acid	Negative	Negative
Blood	Negative	Negative
Leukocyte esterase	Negative	Negative
Red blood cell/HPF	1	0-3
White blood cell/HPF	1	0-5

DISCUSSION

Etodolac is a nonsteroidal anti-inflammatory drug with relatively high selectivity for cyclooxygenase-2 (COX-2) (5). It is primarily metabolized in the liver through hydroxylation and glucuronidation and is excreted mainly via the kidneys in urine, with a smaller proportion eliminated through the bile.

The reaction of bilirubin with diazotized sulfanilic acid, known as the diazo (Van den Bergh) reaction, was introduced by Van den Bergh in 1918 and is widely used for the quantitative measurement of bilirubin in serum and urine. In this reaction, two isomeric colored azo pigments are formed, exhibiting maximum absorbance at 530 nm. The intensity of the resulting color is directly proportional to the bilirubin concentration (6).

Numerous conditions that interfere with urinary bilirubin measurement have been described. For example, ascorbic acid, prolonged storage time, and light exposure may cause false-negative results, whereas the presence of urine-coloring pigments, elevated urobilinogen levels, and various medical therapies may lead to false-positive results. One of the medications known to

cause false-positive urinary bilirubin results is etodolac (7). In such cases, electron-rich regions of the phenolic ring may be attacked by the electrophilic diazonium salt, resulting in the formation of a colored product.

Sho et al. analyzed urine samples from patients with normal serum bilirubin levels but positive urinary bilirubin results using high-performance liquid chromatography (HPLC). Three positive fractions were obtained following extraction of etodolac metabolites with ethyl acetate. The HPLC retention times of two of these fractions corresponded to the 6-hydroxy and 7-hydroxy derivatives of etodolac metabolites (8). In another case report, a 14-year-old girl exhibited a positive urine dipstick bilirubin result during etodolac treatment (9).

Medical therapies can affect certain clinical chemistry test results, such as complete urinalysis. In cases of unexpected or clinically inconsistent urinalysis findings, medication use should be carefully reviewed, and clinicians should be informed about the possibility of false-positive or false-negative results. In patients with unexplained urinary bilirubin positivity and normal liver function test results, etodolac therapy should be considered as a potential interfering factor. This approach may help prevent unnecessary additional testing and invasive procedures. Furthermore, the duration of false-positive urinary bilirubin results in patients using etodolac can be determined through follow-up evaluation.

Research Funding

This study did not receive any external funding.

Conflict of Interest

The authors declare no conflicts of interest.

Informed consent was obtained from the participant.

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