Journal of Medical and Health Studies
ISSN: 2710-1452
DOI: 10.32996/jmhs
Journal Homepage: www.al-kindipublisher.com/index.php/jmhs

JMHS
AL-KINDI CENTER FOR RESEARCH AND DEVELOPMENT

| RESEARCH ARTICLE

Non-Steroidal Anti-Inflammatory, Rhabdomyolysis, and Hemolysis: A Rare Complication of Commonly Used Drugs

Dr. Naser Mohamad Mansoor, Consultant Emergency Medicine, Salmaniya Medical Complex, Kingdom of Bahrain
Zain Mohammed Al Muqbel, Medical Student, Royal College of Surgeons (RSCI), Kingdom of Bahrain
Dr. Ali Haider Ali, Accident & Emergency Resident at Slamaniya Medical Complex, Kingdom of Bahrain
Dr. Maryam Mahmood Ali, Accident & Emergency Resident at Slamaniya Medical Complex, Kingdom of Bahrain
Dr. Taiba Aqeel Husain Ali, Senior Resident, Internal Medicine, Salmaniya Medical Complex, Kingdom of Bahrain
Dr. Mohamed Saif Qayed Ahmed Obaid, Senior Resident, Internal Medicine, Salmaniya Medical Complex, Kingdom of Bahrain
Dr. Esra Al-Nateef, Senior Resident, Internal Medicine, Salmaniya Medical Complex, Kingdom of Bahrain
Dr. Ali Ahmed Abdulaiz Omaran Hasan, Accident & Emergency Resident at Slamaniya Medical Complex, Kingdom of Bahrain
Corresponding Author: Dr. Ali Haider Ali, **E-mail**: Alihaiderali97@outlook.com

| ABSTRACT

Nonsteroidal anti-inflammatory drug (NSAID)-induced hemolytic anemia (DIIHA) and rhabdomyolysis is a rare but notable issue, especially for patients with chronic kidney disease (CKD). While NSAIDs are known for causing gastrointestinal and renal effects, hemolysis-elated and muscle necrosis cases are often overlooked. Patients with CKD, who often take numerous medications, have shifts in how drugs are metabolized, making them more vulnerable to these reactions. We present a case of a 33-year-old man, who has no significant medical illness, and who developed DIIHA and rhabdomyolysis, after taking dexketoprofen, requiring dialysis to preserve his renal function. He showed fatigue, abdominal pain, and dark brown urine. Tests showed high creatinine levels, creatine kinase (CK), and low hemoglobin. Blood gas analysis pointed to metabolic acidosis, possibly due to hemolysis and uremia. Stopping dexketoprofen and providing supportive care, like hydration and blood transfusions, led to better health outcomes. This case highlights the importance of monitoring drug use in vulnerable groups and the need for quick identification and treatment of drug-related blood disorders, particularly among high-risk patients.

| KEYWORDS

Non-Steroidal Anti-Inflammatory; Rhabdomyolysis; Hemolysis; Drugs

| ARTICLE INFORMATION

ACCEPTED: 01 March 2025 **PUBLISHED:** 29 March 2025 **DOI:** 10.32996/jmhs.2024.6.2.1

1. Introduction

NSAIDs are often used for relief of pain and inflammation [6] but have known adverse effects, primarily on kidney function and digestive health. Still, blood-related adverse effects, like drug-induced immune hemolytic anemia (DIIHA), are frequently overlooked. DIIHA is an uncommon yet serious issue that leads to the immune system attacking red blood cells, often triggered by NSAIDs. Patients with chronic kidney disease (CKD), due to their reduced kidney function and multiple medications, are especially at risk for NSAID-related problems. Moreover, many medications are noted to cause muscle necrosis and the release of creatinine kinase and myoglobin. Such medications include antipsychotics, tricyclic antidepressants, barbiturates, and antihistamines (3). Although NSAID can lead to muscle necrosis, it is more likely to exacerbate rhabdomyolysis by leading to acute

ischemic tubular necrosis and renal artery vasoconstriction (4). Therefore, the rate of complication with the illness will be higher and with high morbidity and mortality rates (4). This report examines a case of hemolysis caused by dexketoprofen in a CKD patient, underlining the difficulties in diagnosing and treating this uncommon issue in vulnerable groups.

2. Case Study

A 33-year-old, South Asian Male, presented to the Emergency Department (ED) with abdominal pain, diffuse and cramp-like for three days. The patient was initially assessed in a private hospital and given omeprazole, hyoscine, and dexketoprofen Trometamol. The pain started affecting the limbs and lower back with extremely dark urine, hence, the patient decided to come for another evaluation. He does not have any chronic medical illness or surgical history. Patient vitals were as the following:

Heart rate 110 beats per minute.

Blood pressure: 166/110

Oxygen saturation: 99% on Room Air

Temperature: 37.6 degrees.

Respiratory Rate: 18

The patient on examination had diffused abdominal tenderness, mainly the flank region, and reduced bilateral air entry. The rest of the examination was unremarkable. The patient had a sudden onset of urine retention, and a Foley catheter was inserted. The urine was black and thick in color; in image 1, you can note the findings. Abdominal and Chest X-rays were unremarkable. The initial laboratory investigations are as follows in Table 1.

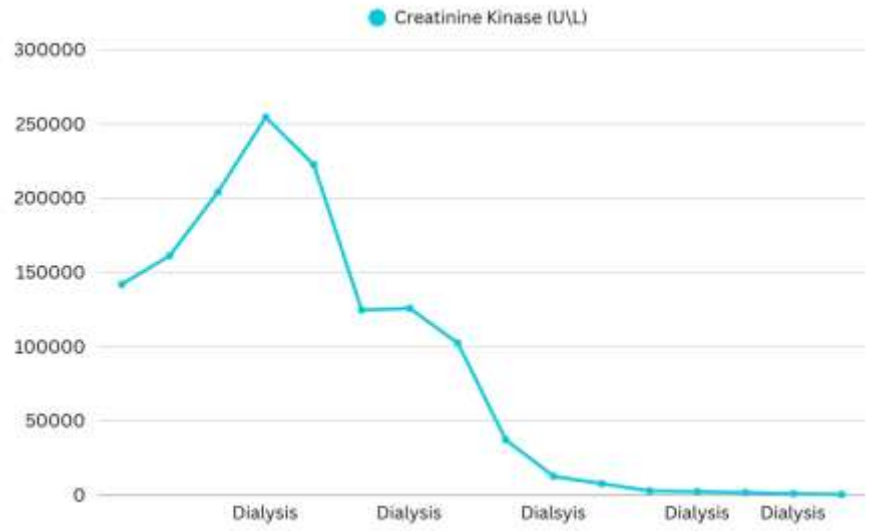
Image 1: Urine after insertion of Foley Catheter.

Table 1: Initial Investigations done in the ED

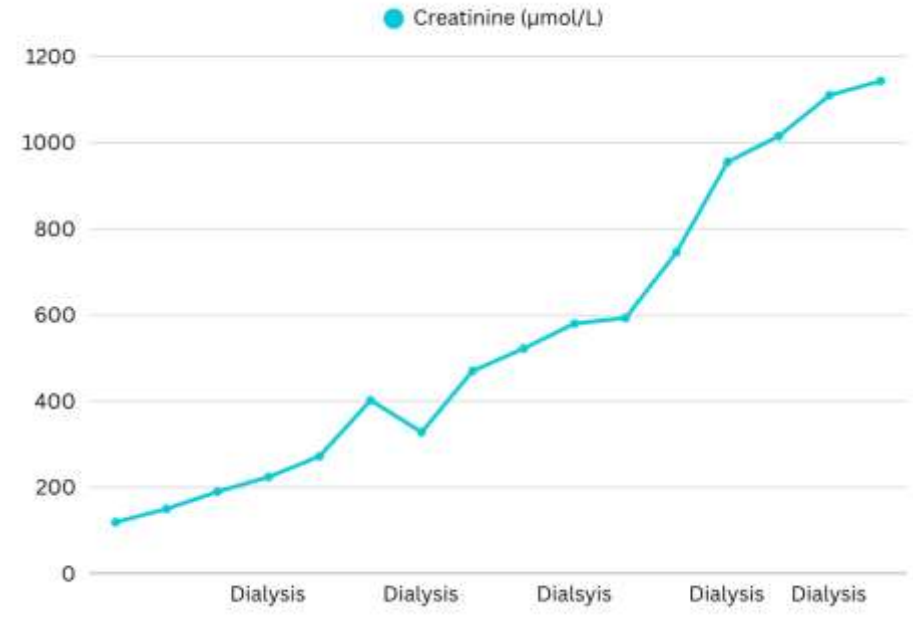
Laboratory Investigation	Value
Hemoglobin	18.6 g\dL
White Blood Cells	16 (80% Neutrophils) x10^9/L
Creatinine	119 µmol/L
Urea	9.0 mmol/L
Creatinine Kinase	141979 U/L
Lactic Dehydrogenase	2180 U/L
Urine Analysis	Myoglobin and Blood +++, otherwise unremarkable.

The patient was in severe rhabdomyolysis, and an abdominal computed tomography was ordered which was expected, with atelectasis changes within the lower Basel area of the lungs. The patient was admitted with acute kidney injury secondary to rhabdomyolysis, which was suspected to be caused by the non-steroidal anti-inflammatory drug (NSAID) given in the initial visit. The patient started to deteriorate during admission with an increase in creatinine and creatinine kinase, associated with an acute drop in hemoglobin. The patient required multiple sessions of dialysis. After two weeks, the patient opted to travel back to his original country for further assessment and treatment. The patient had good urine output at discharge although, renal function was deteriorating. Graphs 1, 2, and 3 show the following trend and findings noted.

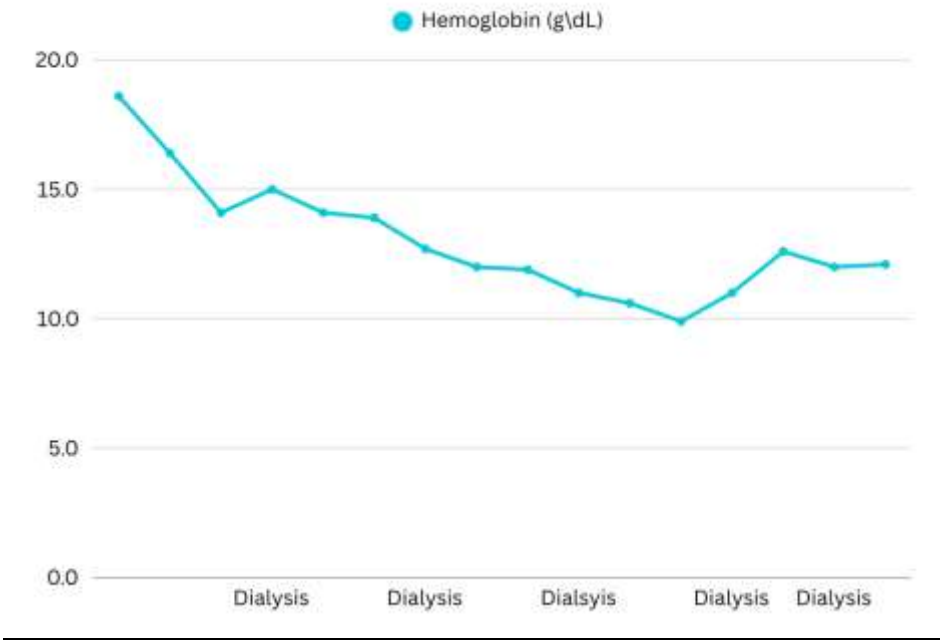
Graph 1: Creatinine Kinase Trend in Association with Dialysis.



Graph 2: Creatinine Trend in Association with Dialysis.



Graph 3: HemglobinTrend in Association with Dialysis.



3. Discussion

Pathogenesis of NSAID-Induced Hemolysis:

Drug-induced hemolysis can occur through immune-mediated or non-immune-mediated mechanisms.

Immune-mediated hemolysis:

NSAIDs, such as dexketoprofen, can cause the body to make drug-dependent antibodies (DDABs). These antibodies attach to red blood cell markers in the presence of the drug, leading to complement activation and the breakdown of red blood cells inside blood vessels. This condition may be confirmed with a positive Direct Antigen Test (DAT) [1]. Most cases of drug-induced immune hemolytic anemia (DIIHA) are from DDABs, which work only when the drug is present. On the other hand, drug-independent antibodies (DIAB) can cause hemolysis even without the drug, similar to warm autoimmune hemolytic anemia (WAIHA). It is important to distinguish between DDAB and DIAB because stopping the drug is necessary for DDAB, while DIAB might also require steroids.

Oxidative Hemolysis:

NSAIDs can create oxidative stress on red blood cells, especially in people with preexisting conditions like chronic kidney disease (CKD) or certain enzyme deficiencies, such as G6PD deficiency [2]. This stress makes red blood cells more fragile, increasing their chance of damage.

Uremic Toxins and CKD:

In people with CKD, uremic toxins can induce oxidative stress and change how drugs are processed, thereby affecting the health of red blood cells. The mix of uremia from CKD and NSAID use dramatically increases the risk of hemolysis [3].

Rhabdomyolysis and NSAID:

Although such side effects are extremely rare, some cases have been reported (8). Usually, it has been noted to be seen in patients with diabetes and its complications, chronic kidney disease, and other high-risk comorbidities (7). The mechanism was noted to be more severe due to NSIAD-related tubular necrosis (7). Moreover, patients were more likely to develop complications with rhabdomyolysis due to the multiple effects of the drug. Although in most cases, rhabdomyolysis can be treated with rest and aggressive fluid therapy, it can be noted that if NSIAD was the culprit, the risk of acute kidney injury and the overall need for dialysis is higher in this group of patients (9). It is also important to note that most athletes may use NSAIDs for muscle aches after exercise, therefore categorizing them as high-risk patients as they are more likely to get rhabdomyolysis and, thus, the risk of acute kidney injury is present (9).

Clinical Perspectives on NSAID Use in CKD

This case highlights that doctors must be careful when giving NSAIDs to CKD patients. More inadequate kidney function results in drug half-lives being extended and plasma levels being higher, increasing the chance of side effects. The patient taking both dexketoprofen and loxoprofen shows the dangers of polypharmacy in CKD situations. Taking more than one NSAID can cause more harmful effects, hence it's essential to review medications and watch patients closely in these risky groups.

Diagnostic Challenges in NSAID-Induced Hemolysis

DIIHA is frequently not diagnosed because it occurs rarely and has vague symptoms. The timing of NSAID usage and signs of hemolysis, along with lab results like high LDH, low haptoglobin, and hemoglobin in urine, are significant for diagnosis. Direct antigen testing (DAT) is key to confirming an immune-related cause. It is critical to distinguish DDAB and DIAB for treatment, as DDAB only needs to stop the drug, while DIAB might also need corticosteroids. Moreover, it is extremely difficult to determine if the cause of the rhabdomyolysis is the medication rather than other etiologies, thus it is a diagnosis of exclusion after excluding all other etiologies (9).

Management Strategies

The primary step in managing DIHHA is to stop the NSAID causing the issue right away. In this situation, stopping dexketoprofen was crucial to prevent further hemolysis. Depending on how severe the hemolysis is, supportive measures like hydration, blood transfusions, and corticosteroids may be necessary. For patients with CKD, continuous dialysis is essential for removing waste products and stabilizing metabolic issues [4].

Key Clinical Takeaways:

- NSAIDs should be avoided in high-risk populations, such as CKD patients, unless necessary.
- Educating patients about the risks of self-medication with over-the-counter NSAIDs is critical for prevention.
- Consider alternative analgesics, like acetaminophen, for vulnerable patients to reduce risk.
- Always use NSAIDs cautiously in high-risk patients such as athletes and CKD to avoid such complications.

Implications for Clinical Practice

This case shows how critical pharmacovigilance is for NSAID use, particularly in patients with CKD and other health issues. The possibility of drug-related blood reactions in these patients means that NSAID prescriptions must be done carefully and precisely. Furthermore, this case emphasizes the necessity for teamwork between nephrology, hematology, and internal medicine experts to ensure prompt diagnosis and effective treatment.

4. Conclusion

This case demonstrates the potentially life-threatening effects of NSAID-induced hemolytic anemia (DIIHA) and rhabdomyolysis in patients with chronic kidney disease. Even though rare, hematologists should be aware of the most common drugs and characteristics causing the often severe and sometimes fatal hemolytic anemia [4]. Unfortunately, reaching the correct diagnosis is not straightforward, even when there is a direct relationship to a specific drug. Early recognition, cessation of the offending drug, and targeted supportive care were key to halting the hemolytic process and preventing further complications. Given the widespread use of NSAIDs, additional research is necessary to better understand the genetic and biochemical factors that predispose patients to DIIHA, paving the way for more personalized and safer treatment strategies. This case emphasizes the need for improved pharmacovigilance and underscores the crucial role of a multidisciplinary approach in managing high-risk patients.

Funding: This research received no external funding.
Conflicts of Interest: The authors declare no conflict of interest.
Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers.

References

[1] Garratty, G. (2009). Drug-induced immune hemolytic anemia. *Hematology, American Society of Hematology Education Program*, 73-79. https://doi.org/10.1182/asheducation-2009.1.73

[2] Johnson, S. T., Fueger, J. T., & Gottschall, J. L. (2007). Drug-induced immune hemolytic anemia: mechanisms and associations. *Transfusion*, 47(4), 697-702. https://doi.org/10.1111/j.1537-2995.2007.01287.x

[3] Esteves, A., Teixeira da Silva, F., & Carvalho, J. (2021). Diclofenac-induced immune hemolytic anemia: A rare but serious adverse reaction. *Cureus*, 13(4), e14006. https://doi.org/10.7759/cureus.14006

[4] Garratty, G. (2010). Immune hemolytic anemia associated with drug therapy. *Blood Reviews*, 24(6), 301-308. https://doi.org/10.1016/j.blre.2010.05.002

[5] Vélez, S. M., Hernández, J. J. R., Davis, S. M., Almodóvar, M. G., & Mercado, J. R. (2016). NSAIDs Prescription Prevalence after a Cardiovascular Event Related Hospitalization in Medicaid Beneficiaries from Puerto Rico. PubMed. https://pubmed.ncbi.nlm.nih.gov/27898167

[6] Larbi, E.B. "Drug-Induced Rhabdomyolysis." *Annals of Saudi Medicine*, vol. 18, no. 6, Nov. 1998, pp. 525–530, https://doi.org/10.5144/0256-4947.1998.525. Accessed 15 Dec. 2020.

[7] "Rhabdomyolysis: Prolonged and High-Intensity Exercises, Impact on Renal Function." *Oatext.com*, 2015, www.oatext.com/rhabdomyolysis-prolonged-and-high-intensity-exercises-impact-on-renal-function.php. Accessed 20 Mar. 2025.

[8] Wichardt, Emma, et al. "Rhabdomyolysis/Myoglobinemia and NSAID during 48 H Ultra-Endurance Exercise (Adventure Racing)." *European Journal of Applied Physiology*, vol. 111, no. 7, 23 Dec. 2010, pp. 1541–1544, https://doi.org/10.1007/s00421-010-1774-2. Accessed 7 Dec. 2021.