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# MEDICATION-ASSOCIATED HYPERURICEMIA AND INCREASED PROTEINURIA FOLLOWING CONCOMITANT USE OF HYDROCHLOROTHIAZIDE-BASED ANTIHYPERTENSIVE THERAPY AND DAPAGLIFLOZIN IN A PATIENT WITH TYPE 2 DIABETES MELLITUS: A CASE REPORT

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**Abstract:**

***Background:*** *Medication-related adverse effects are common in patients with diabetes and hypertension receiving multiple drugs. Hydrochlorothiazide-containing antihypertensive medications may increase serum uric acid levels, while careful renal monitoring is recommended in patients receiving dapagliflozin.*

***Case Presentation:*** *A 60-year-old female with a history of type 2 diabetes mellitus, hypertension, and dyslipidemia presented with intermittent giddiness. During follow-up evaluation, laboratory investigations revealed elevated serum uric acid (7.5 mg/dL) and an increased urine protein-creatinine ratio (0.45). The patient was receiving a hydrochlorothiazide-based antihypertensive regimen along with dapagliflozin. After reviewing the medication profile, the hydrochlorothiazide-containing therapy was discontinued and replaced with an alternative antihypertensive combination. The patient was advised adequate hydration and regular monitoring of renal function and metabolic parameters.*

***Conclusion:*** *This case highlights the importance of routine monitoring for hyperuricemia and proteinuria in patients receiving hydrochlorothiazide-based antihypertensive therapy with dapagliflozin. Early identification and timely modification of therapy can help prevent further renal complications and improve patient outcomes.*

***Keywords:*** *Hyperuricemia, Proteinuria, Hydrochlorothiazide, Dapagliflozin, Type 2 Diabetes Mellitus, Adverse Drug Reaction, Case Report.*

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## INTRODUCTION:

Type 2 diabetes mellitus is one of the most common chronic diseases worldwide and is frequently associated with hypertension and dyslipidemia. As people live longer, many patients require several medications to control blood glucose, blood pressure, and cholesterol levels. Although these medicines improve quality of life and reduce the risk of heart attacks, strokes, and kidney disease, taking multiple drugs together also increases the possibility of adverse drug reactions and drug-related complications.[1] Elderly patients are particularly vulnerable because age-related changes in kidney function and metabolism can alter the way medicines are handled by the body. Therefore, regular clinical assessment and periodic laboratory investigations are essential to identify medication-related problems early and ensure that treatment remains both safe and effective.[2]

Hydrochlorothiazide is a commonly prescribed thiazide diuretic used in combination with other antihypertensive medicines to achieve better blood pressure control. It works by helping the kidneys remove excess sodium and water from the body, thereby lowering blood pressure. Despite its proven effectiveness, hydrochlorothiazide is known to reduce the excretion of uric acid through the kidneys, which can lead to elevated serum uric acid levels.[3] Persistent hyperuricemia may increase the risk of gout, kidney stones, and further deterioration of kidney function, especially in patients with diabetes or pre-existing renal disease. Because these complications may initially remain asymptomatic, routine monitoring of serum uric acid and renal parameters is recommended in patients receiving long-term hydrochlorothiazide therapy.[4]

Dapagliflozin, a sodium-glucose cotransporter-2 (SGLT2) inhibitor, has become an important medication for treating type 2 diabetes mellitus because it not only lowers blood glucose but also provides cardiovascular and renal protection. It acts by increasing urinary glucose excretion, helping improve glycaemic control while reducing the risk of heart failure and slowing the progression of chronic kidney disease[5]. However, because it acts directly on the kidneys, careful monitoring is still necessary, particularly when it is used together with diuretics or other medications affecting renal function. In susceptible patients, dehydration, changes in renal hemodynamics, urinary tract infections, or alterations in urinary protein excretion may occur, making individualized patient assessment and follow-up essential during treatment.[6]

The present case describes a 60-year-old woman with long-standing type 2 diabetes mellitus, hypertension, and dyslipidemia who developed hyperuricemia and an increased urine protein-creatinine ratio while receiving concomitant therapy with a hydrochlorothiazide-based antihypertensive regimen and dapagliflozin. Although the patient initially presented with giddiness, routine laboratory evaluation identified important metabolic and renal abnormalities that prompted a detailed medication review. The hydrochlorothiazide-containing antihypertensive therapy was subsequently discontinued and replaced with an alternative regimen to minimize further renal and metabolic risk. This case emphasizes the importance of regular laboratory monitoring, timely recognition of medication-associated adverse effects, and multidisciplinary collaboration, including clinical pharmacist involvement, to optimize therapy and improve patient safety in individuals receiving multiple long-term medications.[7,8]

## CASE PRESENTATION:

### Patient Demographics

A 60-year-old female presented to the Department of Internal Medicine of a tertiary care teaching hospital on 27 May 2026 with complaints of intermittent giddiness for two days. She weighed 59 kg and was hemodynamically stable at presentation. Her vital signs included a blood pressure of 136/73 mmHg, pulse rate of 68 beats/minute, oxygen saturation of 99% on room air, and normal body temperature.

### Chief Complaints

The patient presented with the following complaints:

- Giddiness on and off for the past two days.
- History of bleeding from the gums approximately two weeks before presentation.

### History of Present Illness

The patient was apparently well until two days before presentation when she developed intermittent episodes of giddiness that were aggravated by changes in head position. The episodes were not associated with loss of consciousness, tinnitus, hearing impairment, nausea, vomiting, limb weakness, or speech abnormalities. Approximately two weeks before hospital presentation, she had experienced an episode of bleeding gums, which resolved without hospitalization. Because of persistent dizziness, she sought medical evaluation.

Initial clinical assessment suggested benign paroxysmal positional vertigo (BPPV). Baseline laboratory investigations demonstrated acceptable hematological and renal parameters, including

hemoglobin of 10.0 g/dL, platelet count of 1.50 lakh/mm³, serum creatinine of 1.29 mg/dL, serum calcium of 9.3 mg/dL, fasting blood glucose of 149 mg/dL, and postprandial blood glucose of 222 mg/dL. She was prescribed betahistine (Vertin® 16 mg) and advised further investigations including HbA1c, ferritin, total iron-binding capacity, liver function tests, urine protein-creatinine ratio (UPCR), vitamin D, vitamin B12, coagulation profile, and dental consultation.

During follow-up after two days, laboratory evaluation revealed HbA1c of 7.3%, elevated UPCR of 0.45, and subsequently serum uric acid of 7.5 mg/dL. Although liver function tests, ferritin, vitamin D, and vitamin B12 levels remained within acceptable limits, the elevated urinary protein excretion and hyperuricemia raised concerns regarding possible medication-associated renal and metabolic effects. The treating physician reviewed her ongoing antihypertensive regimen and discontinued the hydrochlorothiazide-containing fixed-dose combination, replacing it with an olmesartan-amlodipine combination while continuing close follow-up.

**Past Medical History**

The patient had a significant history of chronic metabolic and cardiovascular disorders.

- Type 2 Diabetes Mellitus for approximately 10 years.
- Hypertension for approximately 5 years.
- Dyslipidemia on regular lipid-lowering therapy.

**Past Surgical History**

No previous surgical procedures or hospitalizations were documented in the available medical records.

**Medication History**

At presentation, the patient was receiving the following long-term medications:

| Medication | Dose | Indication |
|---|---|---|
| Sitara-M (Sitagliptin + Metformin) | 100/500 mg once daily | Type 2 Diabetes Mellitus |
| Triolmezest | 40 mg once daily | Hypertension |
| Rosuvas (Rosuvastatin) | 20 mg at bedtime | Dyslipidemia |
| Met XL (Metoprolol Succinate) | 50 mg at bedtime | Hypertension |
| Oxra (Dapagliflozin) | 10 mg once daily | Type 2 Diabetes Mellitus |

**Family History**

No significant family history of diabetes mellitus, hypertension, chronic kidney disease, cardiovascular disease, gout, autoimmune disorders, or hereditary illnesses was documented in the available clinical records.

**Social History**

The patient did not report alcohol consumption, cigarette smoking, tobacco chewing, or recreational drug use. She was independent in activities of daily living and was compliant with regular outpatient follow-up and prescribed medications. No recent travel history or exposure to environmental toxins was documented.

**Occupational History**

The patient's occupation was not documented in the hospital records. There was no available evidence of occupational exposure to nephrotoxic chemicals, heavy metals, industrial solvents, or other hazardous substance

**Allergy History**

The patient had no known drug allergies or documented food or environmental allergies. There was no previous history of hypersensitivity reactions to medications

**Physical Examination**

**General Examination**

The patient was conscious, alert, cooperative, and oriented to time, place, and person. She was afebrile and appeared clinically stable.

**Vital Signs at Presentation**

| Parameter | Finding |
|---|---|
| Temperature | Normal |
| Pulse Rate | 68 beats/minute |
| Blood Pressure | 136/73 mmHg |
| Oxygen Saturation | 99% (Room Air) |

No pallor, cyanosis, clubbing, pedal edema, icterus, or lymphadenopathy was documented. Cardiovascular, respiratory, abdominal, and neurological examinations were unremarkable except for positional vertigo, leading to a provisional diagnosis of benign paroxysmal positional vertigo (BPPV).

**Laboratory Investigations**

**Table 1. Baseline Laboratory Investigations (23–27 May 2026)**

| Investigation | Result | Reference Range | Interpretation |
|---|---|---|---|
| Hemoglobin | 10.0 g/dL | 12–16 g/dL | Mild anemia |
| Total Leukocyte Count | 7030 cells/mm³ | 4,000–11,000 | Normal |
| Platelet Count | 1.50 lakh/mm³ | 1.5–4.5 lakh/mm³ | Normal |
| Serum Calcium | 9.3 mg/dL | 8.5–10.5 | Normal |
| Serum Creatinine | 1.29 mg/dL | 0.6–1.2 | Borderline elevated |
| Fasting Blood Sugar | 149 mg/dL | <126 mg/dL | Elevated |
| Postprandial Blood Sugar | 222 mg/dL | <180 mg/dL | Elevated |

**Table 2. Follow-up Laboratory Investigations (29 May 2026)**

| Investigation | Result | Reference Range | Interpretation |
|---|---|---|---|
| HbA1c | 7.3% | <7% | Suboptimal glycemic control |
| Ferritin | 57 ng/mL | Normal | Normal |
| Total Iron Binding Capacity | 341 µg/dL | Normal | Normal |
| Urine Protein-Creatinine Ratio | 0.45 | <0.20 | Increased proteinuria |
| Total Bilirubin | 0.66 mg/dL | Normal | Normal |
| Direct Bilirubin | 0.14 mg/dL | Normal | Normal |
| SGOT | 21 IU/L | Normal | Normal |
| SGPT | 15 IU/L | Normal | Normal |
| Alkaline Phosphatase | 85 U/L | Normal | Normal |
| Total Protein | 8.1 g/dL | 6–8 | Mildly elevated |
| Albumin | 4.3 g/dL | Normal | Normal |
| Globulin | 3.8 g/dL | Normal | Normal |
| Vitamin D | 45.59 ng/mL | Sufficient | Normal |
| Vitamin B12 | 1400 pg/mL | 222–1439 | High-normal |
| Serum Uric Acid | 7.5 mg/dL | 2.6–6.0 | Hyperuricemia |

These laboratory findings, particularly the elevated urine protein-creatinine ratio (0.45) and serum uric acid (7.5 mg/dL) in a patient receiving dapagliflozin and a hydrochlorothiazide-containing antihypertensive regimen, prompted medication review and modification.

**DIAGNOSIS**

The final diagnosis was medication-associated hyperuricemia and increased proteinuria following concomitant use of a hydrochlorothiazide-based antihypertensive regimen (Triolmezest) and dapagliflozin in a patient with long-standing type 2 diabetes mellitus, hypertension, and dyslipidemia. The patient initially presented with intermittent giddiness and was diagnosed with benign paroxysmal positional vertigo; however, follow-up investigations revealed elevated serum uric acid (7.5 mg/dL) and an increased urine protein-creatinine ratio (0.45) despite stable serum creatinine. After excluding other likely causes and reviewing the patient's medication profile, the hydrochlorothiazide-containing antihypertensive therapy was considered the most probable contributor, with concomitant dapagliflozin potentially influencing renal hemodynamics. Discontinuation of the hydrochlorothiazide-containing regimen and substitution with an alternative antihypertensive combination, along with continued monitoring, constituted the final therapeutic approach.

**TREATMENT**

The patient initially presented with intermittent giddiness and was clinically diagnosed with benign paroxysmal positional vertigo (BPPV). Symptomatic treatment was initiated with betahistine (Vertin 16 mg) twice daily for five days to relieve vertigo. Simultaneously, comprehensive laboratory investigations, including glycated hemoglobin (HbA1c), ferritin, total iron-binding capacity, liver function tests, urine protein-creatinine ratio (UPCR), serum vitamin D, vitamin B12, coagulation profile, and dental consultation, were advised to evaluate the history of gum bleeding and identify any underlying metabolic or systemic abnormalities. The patient was instructed to return for follow-up with the investigation reports for further evaluation and management.

During follow-up, laboratory investigations revealed an elevated urine protein-creatinine ratio (0.45) and hyperuricemia (serum uric acid 7.5 mg/dL), raising suspicion of a medication-associated adverse effect in the setting of concomitant hydrochlorothiazide-based antihypertensive therapy (Triolmezest) and

dapagliflozin. Following medication review, the hydrochlorothiazide-containing antihypertensive regimen was discontinued and replaced with Olmezest-AM (olmesartan 40 mg/amlodipine 5 mg) to maintain blood pressure control while minimizing the risk of further hyperuricemia. Antidiabetic therapy with Sitara-M and dapagliflozin (Oxra), along with metoprolol and rosuvastatin, was continued. The patient was advised to maintain adequate hydration, monitor for symptoms of urinary or genital infections, and undergo regular follow-up assessment of renal function, serum uric acid, urinary protein excretion, blood pressure, and glycemic control to evaluate treatment response and prevent disease progression.

## DISCUSSION

The present case highlights the importance of recognizing medication-related metabolic abnormalities in patients receiving multiple drugs for chronic diseases. Although the patient initially presented with giddiness and was diagnosed with benign paroxysmal positional vertigo, follow-up investigations revealed hyperuricemia and increased urine protein-creatinine ratio, prompting a review of her medications. Hydrochlorothiazide is a well-recognized cause of elevated serum uric acid because it reduces renal uric acid excretion, particularly in patients with diabetes and hypertension. Timely identification of these laboratory abnormalities allowed early modification of antihypertensive therapy before clinically significant renal complications developed. Similar observations regarding hydrochlorothiazide-associated alterations in uric acid metabolism have been reported by Tatsuo Hosoya and colleagues and by Kiichiro Fujisaki and colleagues.[9,10]

Patients with long-standing diabetes frequently require combination therapy to manage blood glucose, blood pressure, and cardiovascular risk factors. While dapagliflozin has consistently demonstrated renal and cardiovascular benefits in large clinical studies, clinicians should remember that changes in renal function and urinary findings can occur during treatment, particularly when combined with diuretics or in susceptible individuals. In this patient, the coexistence of diabetes, hypertension, and polypharmacy may have increased vulnerability to medication-associated renal changes. The decision to discontinue the hydrochlorothiazide-containing regimen while maintaining dapagliflozin with close monitoring represented a balanced clinical approach. This management strategy is consistent with evidence from the DIAMOND trial and the physiological study by David C. H. Wheeler and collaborators demonstrating careful renal monitoring during SGLT2 inhibitor therapy.[11,12]

This case also emphasizes the value of regular laboratory surveillance and multidisciplinary medication review in patients with chronic illnesses receiving multiple medications. Hyperuricemia may remain asymptomatic for prolonged periods but can contribute to gout, nephrolithiasis, and progressive kidney dysfunction if left untreated. Early recognition of elevated serum uric acid and proteinuria enabled prompt modification of therapy, likely reducing the patient's future renal risk. Clinical pharmacists have an important role in detecting potential adverse drug reactions, reviewing medication combinations, educating patients, and recommending appropriate monitoring. Similar conclusions regarding the relationship between hyperuricemia and kidney disease progression have been reported in systematic reviews by Tahir Kanji and by Yuxuan Qiu and colleagues.[13,14]

## CONCLUSION:

This case highlights the importance of recognizing medication-associated metabolic and renal adverse effects in patients receiving multiple therapies for chronic diseases such as type 2 diabetes mellitus, hypertension, and dyslipidemia. The development of hyperuricemia and an increased urine protein-creatinine ratio during concomitant treatment with a hydrochlorothiazide-based antihypertensive regimen and dapagliflozin emphasized the need for careful medication review and routine laboratory monitoring. Early identification of these abnormalities enabled prompt modification of antihypertensive therapy, potentially preventing further renal impairment and long-term complications. This case reinforces the value of individualized pharmacotherapy, regular assessment of renal function and serum uric acid, and the active involvement of clinical pharmacists in detecting adverse drug reactions, optimizing medication regimens, and improving patient safety and therapeutic outcomes.

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