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A Case Report

Familial Renal Glycosuria Presenting with Longstanding Asymptomatic Glycosuria and New-Onset Ketonuria and Bilirubinuria: A Case Report

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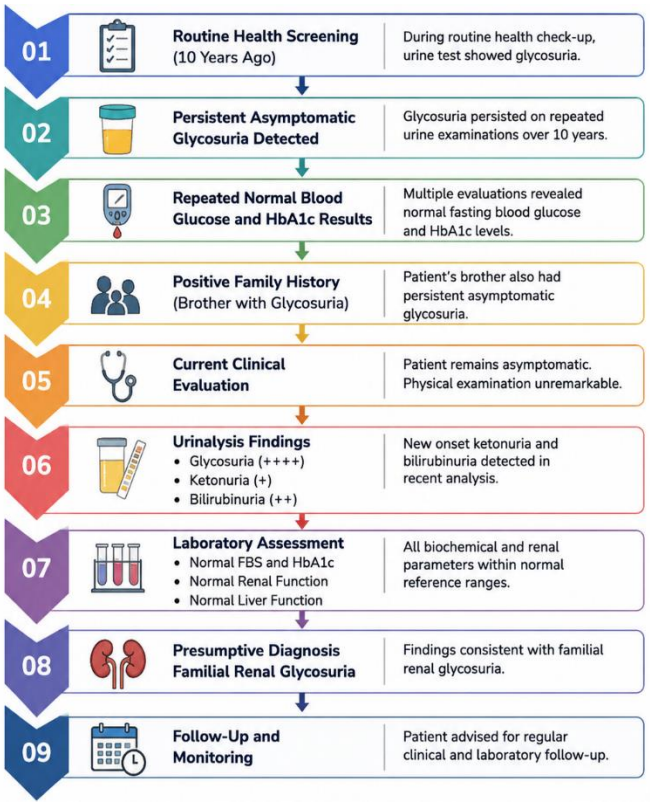
INTRODUCTION

Glycosuria, defined as the presence of glucose in the urine, is most commonly associated with hyperglycemia resulting from diabetes mellitus or other metabolic disorders. Under normal physiological conditions, filtered glucose is almost completely reabsorbed in the proximal renal tubules through sodium-glucose cotransporters, resulting in negligible urinary glucose excretion. Therefore, persistent glycosuria in the presence of normal blood glucose levels is an uncommon finding that warrants further clinical evaluation to identify underlying renal causes [1,2]. Familial renal glycosuria (FRG) is a rare inherited renal tubular disorder characterized by persistent urinary glucose excretion despite normal plasma glucose concentrations and preserved renal function. The condition is most commonly caused by mutations in the SLC5A2 gene, which encodes the sodium-glucose cotransporter-2 (SGLT2) responsible for the majority of renal glucose reabsorption in the proximal tubule [3,4]. Impaired SGLT2 function results in isolated glycosuria without the systemic manifestations typically observed in diabetes mellitus. FRG is generally considered a benign condition and is frequently detected incidentally during routine laboratory investigations [5].The differential diagnosis of isolated glycosuria includes diabetes mellitus, Fanconi syndrome, renal tubular disorders, pregnancy, and drug-induced glycosuria, particularly in individuals receiving sodium-glucose cotransporter-2 inhibitors. Careful clinical assessment and laboratory evaluation are therefore essential to distinguish FRG from other pathological conditions that may require specific treatment or long-term monitoring [6,7].Most reported cases of familial renal glycosuria remain asymptomatic throughout life and demonstrate stable renal function with an excellent prognosis. However, the occurrence of additional urinary abnormalities may complicate the diagnostic process and raise concerns regarding the presence of concurrent renal, hepatic, or metabolic disorders [8,9]. The appearance of ketonuria or bilirubinuria in patients with longstanding isolated glycosuria has rarely been described in the literature, making such presentations diagnostically challenging [10].Recognition of familial renal glycosuria is important because misinterpretation of glycosuria may result in unnecessary investigations, inappropriate treatment, and patient anxiety. A detailed family history, normal glycemic profile, and preserved renal function can provide important clues toward establishing the diagnosis [11,12].We report a case of a 53-year-old male with a longstanding history of asymptomatic glycosuria and a positive family history suggestive of familial renal glycosuria, who subsequently developed new-onset ketonuria and bilirubinuria despite normal blood glucose levels and preserved renal function. This unusual presentation highlights the diagnostic challenges associated with atypical urinary findings in patients with presumed familial renal glycosuria.

CASE PRESENTATION

A 53-year-old male presented to the outpatient clinic for evaluation of persistent asymptomatic glycosuria that had been repeatedly identified during routine health screening over the preceding 10 years. The patient denied symptoms suggestive of diabetes mellitus, including polyuria, polydipsia, nocturia, weight loss, fatigue, or recurrent urinary tract infections. His medical history was unremarkable except for dyslipidemia, for which he was receiving rosuvastatin. He was a non-diabetic, non-hypertensive individual with no history of renal disease, liver disease, or urinary tract pathology.A notable family history was present, as the patient's brother had also been found to have persistent asymptomatic glycosuria during routine laboratory evaluation. This familial occurrence raised the suspicion of familial renal glycosuria.Physical examination revealed no significant abnormalities. Vital signs were within normal limits, and systemic examination of the cardiovascular, respiratory, abdominal, neurological, and genitourinary systems was unremarkable.Laboratory investigations demonstrated persistent glycosuria (++++) on urine dipstick analysis. Recent urinalysis additionally revealed bilirubinuria (++) and ketonuria (+), findings that had not been present in previous assessments. Urine specific gravity was elevated at 1.035, while urine pH was 5.0. Detailed urinalysis findings are presented in Table 1.Despite marked glycosuria, fasting blood glucose was 91.1 mg/dL and HbA1c was 5.24%, excluding diabetes mellitus as the underlying cause. Renal function remained preserved, with serum creatinine of 1.06 mg/dL, blood urea nitrogen of 14.93 mg/dL, and normal creatinine clearance. Microalbuminuria testing was negative, and urinary amino acid analysis was within normal limits, indicating intact renal tubular function. Biochemical and renal function parameters are summarized in Tables 2 and 3.Liver function tests, including serum bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, serum albumin, and total protein levels, were within normal reference ranges despite the presence of bilirubinuria. The patient's lipid profile was also unremarkable and is presented in Table 4.Based on the presence of persistent isolated glycosuria, normal blood glucose levels, preserved renal function, and a positive family history, a presumptive diagnosis of familial renal glycosuria was made. The emergence of ketonuria and bilirubinuria represented atypical findings and prompted recommendations for continued clinical and laboratory follow-up.

Figure 1. Clinical Timeline of Familial Renal Glycosuria and Recent Laboratory Findings



Timeline illustrating the patient's 10-year history of persistent asymptomatic glycosuria, positive family history, recent emergence of ketonuria and bilirubinuria, and subsequent diagnostic evaluation leading to a presumptive diagnosis of familial renal glycosuria.

Table 1. Urinalysis Findings

Parameter	Result	Reference Range
Color	Light Yellow	Light Yellow
Appearance	Clear	Clear
Specific Gravity	1.035	1.005–1.030
pH	5.0	5.0–8.0
Leukocyte Esterase	Negative	Negative
Nitrite	Negative	Negative
Protein	Negative	Negative
Glucose	++++	Negative
Ketones	+	Negative
Urobilinogen	Normal	Normal
Bilirubin	++	Negative
Hemoglobin	Negative	Negative

Urinalysis demonstrated persistent glycosuria in the absence of proteinuria, hematuria, pyuria, or evidence of urinary tract infection. The patient's most recent evaluation additionally revealed glycosuria (++++) with new-onset ketonuria (+) and bilirubinuria (++).

Table 2. Glycemic and Renal Function Assessment

Parameter	Result	Reference Range
Fasting Blood Glucose	91.10 mg/dL	<100 mg/dL
HbA1c	5.24%	<5.7%
Serum Creatinine	1.06 mg/dL	0.7–1.2 mg/dL
Blood Urea Nitrogen	14.93 mg/dL	7–20 mg/dL
Blood Urea	31.94 mg/dL	16.8–43.2 mg/dL
Uric Acid	4.18 mg/dL	3.5–7.2 mg/dL

Glycemic indices and renal function parameters remained within normal limits despite persistent glycosuria, supporting a diagnosis of isolated renal glycosuria rather than diabetes mellitus or generalized renal dysfunction.

Table 3. Liver Function Tests

Parameter	Result	Reference Range
Serum Albumin	4.80 g/dL	3.5–5.1
Total Protein	7.49 g/dL	6.6–8.3
Globulin	2.70 g/dL	2.0–3.5
Albumin/Globulin Ratio	1.77	1.0–2.0
Alkaline Phosphatase (ALP)	50 U/L	30–120
AST (SGOT)	16.06 U/L	5–40
ALT (SGPT)	17.56 U/L	5–45
Total Bilirubin	0.81 mg/dL	0.3–1.1
Direct Bilirubin	0.23 mg/dL	0.1–0.4
Indirect Bilirubin	0.58 mg/dL	0.2–0.8

Liver function parameters were within normal reference limits despite the presence of bilirubinuria on urinalysis,

Table 4. Lipid Profile

Parameter	Result	Reference Range
Total Cholesterol	129.57 mg/dL	≤200
Triglycerides	69.91 mg/dL	<150
HDL Cholesterol	40.98 mg/dL	≥40
LDL Cholesterol	77.61 mg/dL	<100
VLDL Cholesterol	17.44 mg/dL	<50
LDL/HDL Ratio	1.89	2.5–3.5
TC/HDL Ratio	3.16	<3.5
Non-HDL Cholesterol	88.60 mg/dL	<130

Lipid profile analysis demonstrated satisfactory lipid control in a patient receiving rosuvastatin therapy, with all major lipid parameters within recommended target ranges.

DISCUSSION

Familial renal glycosuria (FRG) is a rare inherited renal tubular disorder characterized by persistent urinary glucose excretion despite normal blood glucose concentrations and preserved renal function. The condition is primarily attributed to mutations in the SLC5A2 gene, which encodes the sodium-glucose cotransporter-2 (SGLT2) responsible for the reabsorption of filtered glucose in the proximal renal tubules. As a result, affected individuals exhibit varying degrees of glycosuria in the absence of diabetes mellitus or generalized renal tubular dysfunction [13,14].The present case describes a 53-year-old male with a 10-year history of persistent asymptomatic glycosuria and a positive family history suggestive of familial renal glycosuria. The diagnosis was supported by normal fasting blood glucose, normal HbA1c levels, preserved renal function, and the absence of other features suggestive of Fanconi syndrome or systemic metabolic disease. Similar presentations have been reported in previous studies, where patients with FRG were identified incidentally during routine laboratory investigations and remained asymptomatic despite significant urinary glucose loss [15,16].One of the most important findings in this case is the presence of a positive family history. The patient's brother had a similar history of persistent glycosuria, supporting the possibility of a hereditary renal transport defect. Previous investigations have demonstrated that FRG may follow autosomal dominant or autosomal recessive inheritance

patterns depending on the underlying genetic mutation and degree of transporter dysfunction [17]. Recognition of a familial pattern is clinically important because it may help differentiate FRG from acquired causes of glycosuria and reduce unnecessary diagnostic investigations. Another notable aspect of the present case is the persistence of glycosuria over a prolonged period without evidence of deterioration in renal function. Long-term observational studies have demonstrated that most individuals with FRG maintain normal kidney function and experience a benign clinical course [18]. Consistent with these observations, our patient exhibited normal serum creatinine, blood urea nitrogen, and uric acid levels despite a decade-long history of glycosuria. These findings support the view that isolated renal glycosuria is generally not associated with progressive renal impairment.The emergence of ketonuria represents an unusual feature of this case. While ketonuria is commonly associated with diabetes mellitus, fasting, prolonged exercise, low-carbohydrate diets, or metabolic stress, it has rarely been reported in association with familial renal glycosuria. In the present patient, fasting blood glucose and HbA1c remained within normal limits, making diabetes-related ketosis unlikely. It is possible that transient metabolic factors contributed to ketone production; however, the coexistence of persistent glycosuria and new-onset ketonuria warrants continued monitoring and further evaluation [19]. This finding expands the spectrum of urinary abnormalities that may occasionally accompany FRG.Similarly, bilirubinuria was detected during recent urinalysis despite normal liver function tests and serum bilirubin levels. Bilirubinuria is generally considered a marker of hepatobiliary disease, hemolysis, or liver dysfunction. However, no clinical or biochemical evidence of hepatic pathology was identified in this patient. The significance of isolated bilirubinuria in the setting of presumed FRG remains uncertain and has rarely been described in the available literature [20]. Whether this represents a transient laboratory abnormality or a previously underrecognized finding requires further investigation through long-term follow-up and additional case reports.The differential diagnosis of persistent glycosuria includes diabetes mellitus, Fanconi syndrome, proximal renal tubular dysfunction, pregnancy-associated glycosuria, and medication-induced glycosuria resulting from SGLT2 inhibitor therapy. Comprehensive laboratory evaluation in the present case excluded these conditions. The absence of proteinuria, aminoaciduria, phosphaturia, electrolyte disturbances, and metabolic acidosis argued strongly against generalized proximal tubular dysfunction [21]. Therefore, isolated familial renal glycosuria remained the most likely diagnosis.This case highlights the importance of recognizing FRG as a distinct clinical entity. Failure to identify this condition may lead to repeated investigations, inappropriate treatment, and unnecessary patient anxiety. A detailed clinical history, family history, urinalysis, and assessment of glycemic status are essential components of the diagnostic evaluation. In resource-limited settings where genetic testing may not be readily available, careful clinical assessment remains fundamental for establishing a presumptive diagnosis [22]. Overall, the present case contributes to the limited literature on familial renal glycosuria by documenting an unusual presentation involving longstanding asymptomatic glycosuria accompanied by newly detected ketonuria and bilirubinuria. The findings reinforce the generally benign nature of FRG while emphasizing the need for continued clinical surveillance when atypical urinary abnormalities emerge.

Limitations

Genetic testing for SLC5A2 mutations was not available, preventing molecular confirmation of familial renal glycosuria. In addition, the findings are based on a single patient, limiting generalizability. Long-term follow-up is required to determine the clinical significance of the newly detected ketonuria and bilirubinuria.

Conclusion

Familial renal glycosuria should be considered in patients presenting with persistent glycosuria despite normal blood glucose levels, normal HbA1c, and preserved renal function, particularly when a positive family history is present. This case highlights a rare presentation of presumed familial renal glycosuria in a 53-year-old male with longstanding asymptomatic glycosuria accompanied by the recent emergence of ketonuria and bilirubinuria. Despite these atypical urinary findings, comprehensive biochemical evaluation demonstrated normal glycemic control, renal function, and hepatic function. The case underscores the importance of careful clinical assessment and exclusion of secondary causes of glycosuria to avoid unnecessary investigations and misdiagnosis. Increased awareness of familial renal glycosuria and continued follow-up of affected individuals may improve understanding of its clinical spectrum and long-term implications.

Ethical Approval

Ethical approval was not required for this case report because it describes a single patient and does not involve experimental interventions. The report was prepared in accordance with institutional and journal ethical standards.

Patient Consent Statement

Written informed consent was obtained from the patient for publication of this case report and any accompanying clinical information. A copy of the consent form is available for review by the Editor upon reasonable request.

Data Availability Statement

All data generated or analyzed during this study are included within this published article. Additional information is available from the corresponding author upon reasonable request.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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(AI) Disclosure Statement

During the preparation of this manuscript, artificial intelligence (AI)-assisted tools were used solely for language refinement, grammar correction, and manuscript organization. The authors critically reviewed, edited, and verified all content and accept full responsibility for the accuracy, integrity, and originality of the final manuscript.

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Patient Evaluation and Clinical Management: Malaika Aziz

Data Collection: Malaika Aziz

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Final Approval of Manuscript: Malaika Aziz

The author contributed substantially to the conception, data acquisition, interpretation of findings, manuscript preparation, critical revision, and final approval of the manuscript in accordance with the ICMJE authorship criteria.

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