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A CASE REPORT

Longstanding Asymptomatic Glycosuria with Emergent Ketonuria and Bilirubinuria: A Diagnostic Dilemma

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ABSTRACT:

Background: This case report presents a 53-year-old male with a longstanding history of asymptomatic glycosuria, first noted 10 years ago, and recently found to have new-onset ketonuria and bilirubinuria. His blood glucose levels remain normal, and previous laboratory assessments showed no abnormalities, supporting the diagnosis of isolated glycosuria. A similar finding of asymptomatic glycosuria is reported in his brother, raising the suspicion of familial renal glycosuria (FRG), a rare genetic condition often associated with mutations in the renal sodium-glucose co-transporter (SGLT2). This case emphasizes the significance of identifying familial renal glucosuria in patients presenting with isolated glycosuria, particularly when a relevant family history is present. Additionally, it underscores the diagnostic complexities arising from the emergence of ketonuria and bilirubinuria as new clinical feature. Recognizing FRG as a differential diagnosis can help avoid unnecessary testing and interventions, given its generally benign prognosis.

Keywords: Renal glycosuria,ketonuria,bilirubinuria,Sodium glucose cotransporters

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INTRODUCTION:

Glycosuria, the presence of glucose in the urine, is typically associated with elevated blood glucose levels, as seen in diabetes mellitus or other metabolic disorders. However, isolated glycosuria with normal blood glucose levels and preserved renal function is uncommon and may indicate a rare condition known as familial renal glycosuria (FRG)[1,2].FRG is a benign hereditary disorder caused by mutations in the SGLT2 gene (Santer, et al., 2000), which impair glucose reabsorption in the renal tubules[3]. This condition is typically asymptomatic and does not lead to significant renal or metabolic complications (Calado, et al., 2008), but its unusual presentation can lead to diagnostic confusion if not properly recognized. Few reports exist on FRG, and even fewer discuss the occurrence of concurrent metabolic findings, such as ketonuria or bilirubinuria, in FRG patients[4]. Here, we present a case of a 53-year-old male with a longstanding history of asymptomatic glycosuria and a recent emergence of ketonuria and bilirubinuria, alongside a family history suggestive of FRG[5].

CASE REPORT

The patient, a 53-year-old male, presented to the outpatient clinic for evaluation of persistent asymptomatic glycosuria observed in his laboratory findings over the past few years during his regular health checkups. His prior reports showed glycosuria with other laboratory values within normal limits. The latest urine examination report showed glycosuria ++++, as measured by automated dipstick. Additionally, new findings of bilirubnuria ++ and ketonuria + were noted. The urine specific gravity was slightly elevated at 1.035, with a pH of 5. The patient's fasting blood glucose level was 91.1 mg/dL, and his HbA1C was 5.24%. His blood urea nitrogen and creatinine levels were 14.93 and 1.06 mg/dL, respectively. The patient was a non-diabetic, non-hypertensive individual without any manifestations of renal Disease and was regularly taking only rosuvastatin. Interestingly, the patient's brother also had a history of incidental glycosuria on routine screening. Neither a comprehensive examination of the patient's physiological systems nor the physical examination revealed any abnormal findings. Micro albuminuria tests were negative, and the serum urea, creatinine levels, creatinine clearance rate, and urinary amino acid levels were all within normal ranges, suggesting preserved renal tubular function.

Table 1: Physical Examination Findings

Parameter	Observation
Colour	Light Yellow
Turbidity/Deposit	Nil

Table 2: Chemical Examination Findings

Parameter Name	Result	Reference Value
Specific Gravity (SP)	1.030	1.005–1.030
pH	5.5	5.0–8.0
Leukocyte Esterase	Nil	Nil
Nitrite	Negative	Negative
Proteins	Nil	Nil
Sugar	+++	Nil
Ketones	Nil	Nil
Urobilinogen	Normal	Normal
Bilirubin	Nil	Nil
Haemoglobin	Nil	Nil

Table 3: Microscopic Examination Findings

Parameter Name	Result	Reference Value	Unit
Pus Cells	0–5	0–5	/HPF
Red Blood Cells	0–2	0–5	/HPF
Epithelial Cells	0–2	0–5	/HPF
Amorphous	Nil	Nil	/HPF
Casts	Nil	Nil	/LPF
Organisms	Nil	Nil	/HPF
Yeast Cells	Nil	Nil	/HPF
Dead Sperms	Nil	Nil	/HPF
Miscellaneous	Nil	Nil	/HPF
Crystals	Nil	Nil	/HPF

Table 4: Lipid Profile Analysis

Description	Result	Unit	Reference Range	Methodology
Cholesterol – Total	129.57	mg/dL	Desirable: ≤200, Borderline High: 201–239, High Risk: ≥240	CHOD-POD Method
Triglycerides	69.91	mg/dL	Normal: <150, Borderline High: 150–199, High: 200–499, Very High: ≥500	GPO-POD Method
HDL Cholesterol	40.98	mg/dL	Desirable: ≥60, Borderline Low: 40–60, Low (High Risk): <40	Direct Method
LDL Cholesterol	77.61	mg/dL	Optimal: <100, Near Optimal: 100–129, Borderline High: 130–159, High: 160–189	Direct Method
VLDL	17.44	mg/dL	<50	Calculated
LDL/HDL Ratio	1.89	Ratio	2.5–3.5	Calculated
TC/HDL Ratio	3.16	Ratio	<3.5	Calculated
Non-HDL Cholesterol	88.60	mg/dL	<130	Calculated

Table 5: Fasting Blood Sugar (FBS)

Description	Result	Unit	Reference Range	Methodology
Fasting Blood Sugar (FBS)	91.10	mg/dL	Normal: <100, Prediabetes: 100–125, Diabetes: ≥126	GOD-POD

Table 6: HbA1c Analysis

Description	Result	Unit	Reference Range	Methodology
HbA1c	5.24	%	Normal: <5.7%, Prediabetes: 5.7–6.4%, Diabetes: ≥6.5%	Enzymatic Assay Method

Table 7: Liver Function Test (LFT)

Description	Result	Unit	Reference Range	Methodology
Serum Albumin	4.80	g/dL	3.5–5.1	Bromocresol Green
Serum Total Protein	7.49	g/dL	6.6–8.3	Biuret
Serum Globulin	2.70	g/dL	2.0–3.5	Calculated
Albumin/Globulin Ratio	1.77	—	1.0–2.0	Calculated
Alkaline Phosphatase (ALP)	50.00	U/L	30–120	IFCC Modified Method
SGOT (AST)	16.06	U/L	5–40	FCC
SGPT (ALT)	17.56	U/L	5–45	FCC
Indirect Bilirubin	0.58	mg/dL	0.2–0.8	Calculated
Direct Bilirubin	0.23	mg/dL	0.1–0.4	VOX Method
Total Bilirubin	0.81	mg/dL	0.3–1.1	VOX Method

Table 8: Renal Function Panel

Description	Result	Unit	Reference Range	Methodology
Creatinine	1.06	mg/dL	0.7–1.2	Sarcosine Oxidase Method
Urea (Blood)	31.94	mg/dL	16.8–43.2	Urease–GLDH, UV Method
Blood Urea Nitrogen	14.93	mg/dL	7–20	Calculated
Uric Acid	4.18	mg/dL	3.5–7.2	Uricase–Peroxidase Method

DISCUSSION:

Familial renal glycosuria (FRG) is a rare, typically benign, hereditary condition characterized by the persistent excretion of glucose in the urine without the presence of hyperglycemia or generalized renal impairment[6]. This case of a 53-year-old male with a longstanding history of asymptomatic glycosuria adds to the limited body of literature on FRG (Baker,

LR, DM, & EM, 2014) and underscores the clinical relevance of recognizing this genetic condition. The recent detection of ketonuria and bilirubinuria in the patient's urine is notable, as it is not typical of FRG and may suggest an evolving renal or metabolic process warranting further observation[7].In familial renal glycosuria, mutations in the sodium-glucose co-transporter 2 (SGLT2) gene impair renal glucose reabsorption in the proximal tubules, leading to glycosuria without affecting blood glucose levels (Santer, et al., 2000). Since SGLT2 is responsible for most glucose reabsorption in the kidney, its dysfunction selectively results in isolated glycosuria[8]. It is transmitted autosomal recessively (R, C, & WA, 2004). This patient's normal blood glucose levels, HbA1c, and renal function profile align with the classic presentation of FRG. Additionally, the presence of asymptomatic glycosuria in the patient's brother further strengthens the likelihood of a familial pattern and suggests a possible inherited mutation in SGLT2 or a similar transporter gene[9,10]. Familial cases such as this are of interest because they help distinguish FRG from more common causes of glycosuria, such as diabetes mellitus, renal tubular acidosis, or Fanconi syndrome, each of which presents with additional clinical and biochemical features.Current literature indicates that FRG typically does not result in long-term complications, as it is generally asymptomatic and does not lead to significant renal dysfunction (Calado, et al., 2008)[11]. In most cases, FRG does not require treatment beyond monitoring, as it is often benign and self-limiting. However, the discovery of new findings of ketonuria and bilirubinuria in this patient raises questions about potential atypical presentations of FRG or concurrent metabolic disturbances that may evolve over time[12,13]. These findings are unusual in the context of FRG and could represent transient metabolic stress or, less likely, early markers of a secondary condition. To our knowledge, no cases have yet established a direct link between FRG and either ketonuria or bilirubinuria, suggesting a need for further investigation [14-16].

LIMITATIONS:

- Lack of Genetic Testing: A definitive diagnosis of familial renal glycosuria (FRG) typically requires genetic testing to confirm mutations in the SGLT2 gene or other relevant transporters. Without this, the diagnosis remains presumptive based on clinical and family history, which may limit the conclusiveness of the case.
- Single Case Observation: As a single case, this report cannot establish a broader link between FRG and the observed ketonuria or bilirubinuria. The unusual findings may be unique to this individual and may not be generalizable to other FRG patients, limiting the applicability of the findings.
- Lack of Long-Term Follow-Up: Since this case report lacks long-term follow-up data, it cannot determine whether the ketonuria and bilirubinuria represent a transient phenomenon, an early marker of an evolving renal or metabolic condition, or a benign variation within FRG. This limits insights into the prognostic implications of these findings.

CONCLUSION:

This case report presents a unique instance of familial renal glycosuria (FRG) in a 53-year-old male with a history of persistent, asymptomatic glycosuria, now accompanied by new findings of ketonuria and bilirubinuria. This case underscores the importance of considering FRG as a differential diagnosis for isolated glycosuria, particularly when there is a positive family history, to prevent unnecessary testing and misdiagnosis. Clinicians should be aware of FRG's presentation and benign prognosis to ensure appropriate management. Further study of cases with atypical findings, such as ketonuria and bilirubinuria in FRG, may help deepen understanding of its clinical spectrum and implications for patient care.

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Authors Contributions

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Data Collection & Data Analysis: **Malaika Aziz**

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REFERENCES

1.Berrut G, Boureau AS, Trochu JN, Genet B, De DecKer L, Hanon O. Empagliflozin in the elderly. Geriatrie.et psychologie neuropsychiatrie duvieillissement.2021;doi: https://doi.org/10.1684/pnv.2021.0987.

2.Djeddi D, Cauliez A, Oulebsir A, Hureaux M, Vanrenterghem A, Vargas-Poussou R. Persistently high urine glucose levels caused by familial renal glycosuria. Archives de pediatrie : organe officiel de la Societe francaisedepediatrie.2020;27:386-7.doi: https://doi.org/10.1016/j.arcped.2020.07.002.

3. Dorum S, Erdoğan H, Köksoy AY, Topak A, Görükmez Ö. Clinical features of pediatric renal glucosuria cases due to SLC5A2 gene variants. Pediatrics international : official journal of the Japan Pediatric Society.2022;64:e14948.doi: https://doi.org/10.1111/ped.14948.

4.Fathi A, Vickneson K, Singh JS. SGLT2-inhibitors; more than just glycosuria and diuresis. Heart failure reviews.2021;26:623-42.doi: https://doi.org/10.1007/s10741-020-10038-w.

5. González-Albarrán O, Morales C, Pérez-Maraver M, Aparicio-Sánchez JJ, Simó R. Review of SGLT2i for the Treatment of Renal Complications: Experience in Patients with and Without T2D. Diabetes therapy : research, treatment and education of diabetes and related.disorders.2022;13:35-49.doi: https://doi.org/10.1007/s13300-022-01276-2.

6.Kakadiya J, Varsadiya K, Kakadiya C, Prajapati M, Patel P. Hypokalemic Quadriparesis Associated With Renal Glycosuria in Dengue Fever: A Rare Presentation. Cureus.2024;16:e65489.doi: https://doi.org/10.7759/cureus.65489.

7.Lee JH, Kim SA, Jo CH, Lee CH, Kim GH. Urinary Concentration Defect and Renal Glycosuria in Cyclosporine-treated Rats. Electrolyte & blood pressure : E&BP.2020;18:1-9.doi: https://doi.org/10.5049/ebp.2020.18.1.1.

8. Liman MNP, Jialal I. Physiology, Glycosuria. StatPearls. Treasure Island (FL) ineligible companies. Disclosure: Ishwarlal Jialal declares no relevant financial relationships with ineligible companies.:2021;26:623-42. https://doi.org/10.7759/cureus.65489.

9.Mng'agi MO, Mwandigha AM, Mbugi EV. Gender-inclined Young Age Glycosuria: Contribution to Late Age Chronic Renal Diseases, Type 2 Diabetes Mellitus and Cardiovascular Diseases. The East African health researchjournal.2023;7:88-93.doi: https://doi.org/10.24248/eahrj.v7i1.713.

10. Ormonde C, Laranjinha I, Gil C, Gonçalves M, A AG. Glycosuria in primary glomerulopathies: prevalence and prognostic.significance.Jornal.brasileirode nefrologia.2022;44:26-31.doi:https://doi.org/10.1590/2175-8239-jbn-2021-0115.

11. Qu Y, Hao L, Wang X. A young-onset type 2 diabetic Chinese girl with familial renal glycosuria caused by a novel mutation in SLC5A2: A case report. Journal of diabetes.2023;15:622-6.doi:https://doi.org/10.1111/1753-0407.13410.

12. Ren Q, Gong S, Han X, Ji L. Hereditary renal glycosuria, diabetes and responses to SGLT2 inhibitor. Journal.ofdiabetes.2022;14:216-20.doi: https://doi.org/10.1111/1753-0407.13254.

13. Rroji M, Kasa M, Spahia N, Spasovski G, Müller RU. Familial renal glycosuria as a genetic model of long-term SGLT2 inhibition: potential implications for calcium phosphate metabolism.and.bone.health.Journalof nephrology.2025;38:1483-6.doi: https://doi.org/10.1007/s40620-024-02164-7.

14. Sivaji V, Raju P, Marimuthu S, Sundar S. Familial renal glycosuria identified in an Indian family. BMJ case reports.2024;17:doi:https://doi.org/10.1136/bcr-2023-258408.

15. Topaloglu R. Extrarenal complications of cystinosis. Pediatric nephrology (Berlin, Germany). 2024;39:2283-92. doi: https://doi.org/10.1007/s00467-023-06225-0.

16. Zhang P, Xu F, Liu X, Hu Z, Liang D, Liang S, et al. Clinicopathological features and outcomes of PLA2R-related membranous.nephropathy;withrenal.glycosuria. Clinical.nephrology.2024;102:273-84.doi: https://doi.org/10.5414/cn111362.

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