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CASE REPORT

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# Glycogen storage disease in two sisters: A case report

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**Key Clinical Message**

Glycogen storage diseases (GSDs) are rare autosomal disorders that result from defects in glycogen metabolism. There are more than 12 types, each with distinct clinical features. Clinical scenario, biochemical abnormalities are useful for suspicion whereas liver biopsy and enzyme assay provides definite diagnosis. We report a case of two sisters with similar clinical symptoms suggestive of the disease.

**KEYWORDS**

glycogen storage disease, hepatomegaly, hypoglycemia, metabolic

## 1 | INTRODUCTION

The glycogen storage diseases (GSDs) are a diverse group of inherited diseases numbering more than 12, caused by abnormalities of the enzymes involved in the synthesis or degradation of glycogen.[1] GSDs can broadly be divided into those with hepatic involvement, which present as hypoglycemia, and others which are associated with neuromuscular disease and weakness.[2] GSDs is diagnosed on the basis of combination of clinical symptoms, biochemical results, and liver or muscle biopsy along with the specific enzyme assay. We report a case of two sisters with clinical presentation of repeated episodes of hypoglycemia, abdominal distension along with hepatomegaly suggestive of GSDs.

## 2 | CASE REPORT

A 4-year-old female Nepalese child born from non-consanguineous marriage was evaluated for repeated episodes of hypoglycemia. She also had progressive abdominal distension, failure to thrive and history of seizure in the past. History of hypoglycemia started when she was 10 months old and there was one episode of seizure during the same period. She was born full-term with a birth weight of 3000 gm with an uneventful birth history. On examination, her weight was 12 kg and length was 98 cm, both were less than fifth percentile for her age. There was pallor but no icterus. She had hepatomegaly with a liver span of 12 cm, but no splenomegaly or ascites. On admission, the child had fever and cough with documented hypoglycemia (blood sugar 26 mg/dL). No ketone bodies were seen in urine. Blood investigations showed anemia, hyperlipidemia, and hyperuricemia. (Table 1).

Blood gas showed lactic acidosis with a pH of 7.28. Renal function test was within normal limits. Hepatitis B and C serology was normal. ECHO, X-ray chest and fundoscopy examination done in the past were also normal. The child was suspected to have glycogen storage disorder based on gradual abdominal distension, history of convulsions, massive hepatomegaly, hypoglycemia, hypertriglyceridemia, and hypercholesterolemia. Liver biopsy and enzyme assay would have provided definitive diagnosis. However, with regards to the cost and unavailability of absolute treatment options parents denied liver biopsy and enzyme assay despite repeated counseling.

**TABLE 1** Lab parameters.

| Parameter | Value | Reference range (for given age/sex) |
|---|---|---|
| Total leucocyte count | 10,280/$mm^3$ | 4.0–12.0*1000/ $mm^3$ |
| Hemoglobin | 9.5 g/dL | 11.5–14.5 g/dL |
| Platelet count | 513,000/$mm^3$ | 150–400*1000/$mm^3$ |
| Triglyceride | 471 mg/dL | 32–99 mg/dL |
| Serum uric acid | 13 mg/dL | 2.2–4.7 mg/dL |
| Alanine transaminase | 21 U/L | 5–45 U/L |
| Aspartate transaminase | 88 U/L | 15–50 U/L |
| Blood pH | 7.28 | 7.35–7.45 |
| $PCO_2$ | 32 mmHg | 35–45 mmHg |
| $HCO_3$ | 18 mmol/L | 22–28 mmol/L |
| Lactate | 6 mmol/L | 0–0.2 mmol/L |
| HBsAg | Non reactive | - |
| HCV | Non reactive | - |

On further evaluation her 15-month-old younger sister was found to have similar symptoms. She also had repeated episodes of hypoglycemia with blood sugar reaching up to 35 mg/dL and distended abdomen with liver palpable 3 cm below the right subcostal margin with liver span of 11 cm. She was born full term with birth weight 2800 gm with an uneventful birth history. On examination, pallor was present with no other remarkable findings on general and systemic examination. Parents denied any investigations in relation to glycogen storage disease, as there was no specific treatment available in the country.

Both patients were managed with 4 hourly corn starch feeding in between meals and allopurinol was used for the control of hyperuricemia. Both are under regular 3 monthly follow-up and the tendency of hypoglycemia has reduced. They had the last episode of hypoglycemia around 6 months back, when both sisters suffered from flu-like illness. Height, weight, and liver span is measured during each follow-up.

## 3 | DISCUSSION

Glycogen storage disease type I is a rare autosomal recessive metabolic disorder that occurs due to inability to break down glucose 6 phosphate into glucose and phosphate due to deficiency of glucose 6 phosphatase enzyme.[3] Clinical manifestations of type I glycogen storage disease generally occur at 3–6 months of life as hepatomegaly, hypoglycemia, hyperlactatemia, hyperuricemia, and hypertriglyceridemia.[4] However cases have been reported among older children, adolescent as well as adults.[5–7] Our patient had fasting hypoglycemia with hypertriglyceridemia, hyperuricemia, hypercholesterolemia, and random blood sugar responding to oral glucose. The clinical scenario and laboratory parameters are consistent with type Ia GSD (232200). Some of the patients with type I GSD also have mild to severe neutropenia.[8] Total leukocyte count was normal in our patient. Renal manifestations of GSDIa appear in early childhood, the first of which is hyperfiltration followed by microalbuminuria, and hence probably goes undetected without specific diagnostic evaluation.[4] Deranged renal function was more common in older children (age >13 years) with normal studies among younger children in a study by Chen et al.[5] Our patient had normal renal function and there was no evidence of microalbuminuria.

Consanguineous marriage leads to increased expression of autosomal recessive disorder such as GSD.[9] Reported children are from Tamang ethnic group where consanguineous marriage is common; however, two sisters were not born out of consanguineous marriage. Hence both the parents must be the carrier for the disease to be expressed in daughters.

Liver biopsy or quantitative enzyme assay are generally used for the definitive diagnosis of the type I glycogen storage disease. Though advised, the parents denied further investigation due to cost of confirmatory tests like enzymatic or mutational analysis, biopsy and lack of easy access to definitive management in patients with GSDs, which was also pointed out by Pandey AS in her study.[10]

Along with the prevention of acute metabolic derangement as well as acute and long-term complications, attainment of normal psychological development, and quality life is the goal of management. It can only be achieved through early diagnosis. Undiagnosed and untreated children have abnormal cognitive development from recurrent hypoglycemic episodes as well as failure to thrive

with delayed motor development, short stature.[8] Hence symptomatic management should be started based on presumptive diagnosis in resource limited settings where definitive diagnosis cannot be performed early/always.

Key aim is to treat or avoid hypoglycemia, hyperlactatemia, hyperuricemia, and hyperlipidemia. Consuming starch avoids hypoglycemia as its slow digestion results in steady release of glucose. Hyperuricemia and hyperlipidemia may require treatment with allopurinol and statins, respectively.[11] We have started the older sibling on allopurinol and statin for hyperuricemia and hyperlipidemia, respectively.

Long-term consequences of GSDIa if left untreated include growth retardation, delayed puberty, gout, arterial and (rarely) pulmonary hypertension, osteoporosis or osteopenia polycystic ovary syndrome, hepatocellular adenoma (HCA), hepatocellular carcinoma (HCC), chronic renal disease and renal failure, neuropathy, and cognitive delays and epilepsy because of repeated or severe hypoglycemic events.[12] In a review by Bianchi et al. about published cases of HCA in GSD, it was more common in the second decade of life with mean age of 19.8 yrs and in male as opposed to adenoma due to other causes. The mean age of patients with HCC was 23 years with a span of 2–7 years between HCA and HCC.[13]

A large number of cases of inborn error of metabolism is expected considering the incidence of mental retardation, prevalence of consanguinity in some areas of Nepal; however, many cases remain undiagnosed due to a lack of concern toward this group of disorders.[14] This might be true for many low- and middle-income countries. We did not find any reported cases from Nepal despite comprehensive literature review and ours might be the first reported case. This case report can be of significant value to researchers and policy makers of Nepal and other low-income countries related to metabolic disorder.

## 4 | CONCLUSION

Glycogen storage disease should also be suspected while evaluating a case of hepatomegaly or hypoglycemia as there might be some cases of GSDs though not adequately reported. Management of GSDs is a challenge in resource limited settings where liver biopsy and enzyme assay are not readily available or affordable.

## AUTHOR CONTRIBUTIONS

**Sushan Homagain:** Writing – original draft; writing – review and editing. **Sajal Twanabasu:** Conceptualization; writing – original draft; writing – review and editing. **Ram Chandra Rijal:** Writing – review and editing. **Jeevan Ghimire:** Writing – review and editing. **Prabin Duwadee:** Writing – review and editing.

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## CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

## CONSENT

Written informed consent was obtained from the parents to publish this report in accordance with the journal's patient consent policy.

## DATA AVAILABILITY STATEMENT

Data will be provided by the corresponding author on reasonable request.

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