https://doi.org/10.29309/TPMJ/2023.30.10.7667

The Professional Medical Journal
www.theprofesional.com
2023, Volume, 30 Issue, 10

ORIGINAL ARTICLE

Clinical, biochemical and radiological findings in children with glycogen storage disease.

Sasui Anam[1], Arit Parakash[2], Aisha Merchant[3]

Article Citation: Anam S, Parakash A, Merchant A. Clinical, biochemical and radiological findings in children with glycogen storage disease. Professional Med J 2023; 30(10):1324-1327. https://doi.org/10.29309/TPMJ/2023.30.10.7667

ABSTRACT… Objective: To determine the clinical, biochemical and radiological findings in children with glycogen storage disease (GSD) presenting to National Institute of Child Health, Karachi, Pakistan. **Study Design:** Cross-sectional study. **Setting:** Department of Hepatology and Gastroenterology, National Institute of Child Health, Karachi. **Period:** January 2021 to June 2022. **Material & Methods:** A total of 40 children of either gender (male or female) aged ≤ 13 years diagnosed with GSD (confirmed on liver biopsy) were included. Clinical, biochemical and radiological findings were included. Data analysis was performed using SPSS Ver. 26.0. **Results:** In a total of 40 children with GSD, 22 (55.0) were boys. There were 24 (60.0%) children who had age between 1 to 3 years. The mean age, weight and height were 2.8±1.7 years, 10.3±3.5 kg and 79.9±11.6 cm respectively. Abdominal distension and hepatomegaly were the most common presentation reported in 40 (100%) children each while 37 (92.5%) children reported increased appetite. Biochemical investigations revealed that ALT 2 time above upper limit normal, hypertriglyceridemia and hyperuricemia were noted among 37 (92.5%), 32 (80.0%) and 16 (40.0%) children respectively. Liver biopsy had revealed GSD among all cases. **Conclusion:** Abdominal distension, hepatomegaly and increased appetite were the most common clinical presentation among children with GSD. Biochemical investigations revealed that ALT 2 time above upper limit normal, hypertriglyceridemia and hyperuricemia were the most frequent among children with GSD.

Key words: Abdominal Distension, Glycogen Storage Disease, Hepatomegaly, Hypertriglyceridemia, Hyperuricemia.

INTRODUCTION

Glycogen storage diseases (GSD) are genetic disorders of carbohydrate metabolism caused by abnormalities of enzymes that regulate either the synthesis or degradation of glycogen.[1,2] In patients with GSD, glycogen is abnormal in quantity and quality.[2] Given the rare and extensive nature of the GSD, their multiple clinical and radiological traits may seem challenging. Early recognition of GSD is imperative given the availability of new treatment options to prevent irreversible damage.[3]

In a study, clinical characteristics showed that abdominal distension was observed in 83.3% patients, short stature 64.2%, recurrent wheezing 44.4%, diarrhea 40.3%, vomiting 27.8%, and seizures 22.8% patients.[4] Furthermore, laboratory characteristics showed that hypertriglyceridemia was observed in 100%, transeminasemia in 77.5%, anaemia in 38.9%, hypercholesterolemia in 33.3%, metabolic acidosis in 16.6%, and hyperuricemia in 11.7% children with GSD.[4] In another study, radiological characteristics of children with GSD showed like nephromegaly with increased echogenicity in all 5 (100%) children, medullay nephrocalcinosis and stones was observed in 3 (60%) children with GSD.[5]

The determination of most frequent clinical and laboratory characteristics is an indispensable core for the early recognition of rare disease like GSD.[6-8] Moreover, the current study also investigated radiological features of these children. This study was thought to ultimately help the clinician with both diagnosis and prognosis of children with GSD. Objective of this study was to determine the

1. MBBS, Post-Graduate Resident Pediatric Medicine, National Institute of Child Health, Karachi.
2. MBBS, FCPS (Pediatric Medicine), FCPS (Pediatric Gastroenterology), Professor Pediatric Medicine, National Institute of Child Health, Karachi, Pakistan.
3. MBBS, FCPS (Pediatric Medicine), Senior Registrar Pediatric Medicine, National Institute of Child Health, Karachi, Pakistan.

Correspondence Address:
Dr. Sasui Anam
Department of Pediatric Medicine
National Institute of Child Health, Karachi.
dranammahesar123@gmail.com

Article received on: 04/05/2023
Accepted for publication: 10/07/2023

clinical, biochemical and radiological findings in children with GSD presenting to National Institute of Child Health, Karachi, Pakistan.

MATERIAL & METHODS

This cross-sectional study was conducted at Department of Hepatology and Gastroenterology, National Institute of Child Health, Karachi, Pakistan from January 2021 to June 2022. This study was conducted after getting approval from Institutional Ethical Committee (IERB No. 36/2020, dated: 26-11-2020).

Inclusion criteria were all children of either gender (male or female) aged ≤ 13 years diagnosed with GSD presenting to us during the study period. Exclusion criteria were children with other storage disorders. Parents or caregivers of children unwilling to be part of this study were also not included. GSD was described as a metabolic disorder caused by enzyme deficiencies affecting either glycogen synthesis, glycogen breakdown or glycolysis (glucose breakdown), typically within muscles and/or liver cells. It was confirmed on liver biopsy.

Clinical presentation like abdominal distension, hepatomegaly, short stature, dolls facies, diarrhea, convulsion, vomiting and appetite along with biochemical findings like hypertriglyceridemia, transaminasemia, hypercholesterolemia, hyperuricemia and hypoglycemia were noted. Radiological findings like hepatomegaly, nephromegaly and renal stones were also noted. Short stature was labeled as height SDs <-2 for particular age and sex. Doll's facies was labeled as facial appearance with a round facial form, full cheeks, a short nose, and a relatively small chin. Hypertriglyceridemia was defined as presence of triglycerides level of >200 mg/dl. Normal transaminasemia levels were defined as aspartate transaminase [AST] <40 IU/L or alanine transaminase [ALT] <35 IU/L. Hypercholesterolemia was described as total cholesterol level >200 mg/dL. Metabolic acidosis was labeled as pH <7.35 and bicarbonate <24 mEq/L. Neutropenia was labeled as the absolute neutrophil count (ANC) of <1500/mm^3. Nephromegaly was labeled as maximal renal length above the 95th percentile on ultrasound (confirmed on the basis of medical record). Increased echogenicity was defined as fatty infiltration of the liver producing a diffuse increase in echogenicity.

Data analysis was performed using SPSS Ver. 26.0. Mean and standard deviation were calculated for quantitative data whereas frequency and percentages were calculated for demographic features, clinical presentation, biochemical and radiological findings.

RESULTS

In a total of 40 children with GSD, 22 (55.0%) were boys. There were 24 (60.0%) children who had age between 1 to 3 years. The mean age, weight and height were 2.8±1.7 years, 10.3±3.5 kg and 79.9±11.6 cm respectively. Table-I is showing baseline characteristics of children studied.

Characteristics		Number (%)
Gender	Boys	22 (55.0%)
	Girls	18 (45.0%)
Age (years)	<1	7 (17.5%)
	1-3	24 (60.0%)
	>3	9 (22.5%)
Consanguinity	Yes	36 (90.0%)
	No	4 (10.0%)

Table-I. Demographic characteristics of children with glycogen storage disease (n=40)

Abdominal distension and hepatomegaly were the most common presentation reported in 40 (100%) children each while 37 (92.5%) children reported increased appetite. Figure-1 is showing frequency of common clinical presentations among children with GSD.

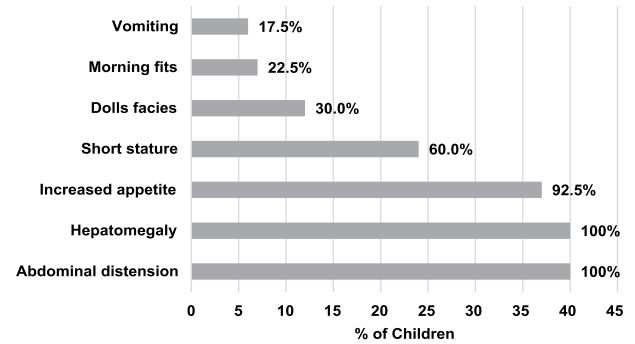

Figure-1. Frequency of common clinical presentations among children with glycogen storage disorders (n=40)

Biochemical Abnormalities	Frequency (%)
Hypertriglyceridemia	32 (80.0%)
Hypercholesterolemia	11 (27.5%)
ALT (>2xULN)	37 (92.5%)
CPK (>170U/L)	3 (7.5%)
Hyperuricemia (>5mg/dl)	16 (40.0%)
Hypoglycemia	4 (10.0%)
Neutropenia	10 (25.0%)
Urinary ketones	12 (30.0%)
Metabolic acidosis	15 (37.5%)

Table-II. Frequency of biochemical abnormalities among children with glycogen storage disorders (n=40)

DISCUSSION

GSD is considered to be a rare group of inherited disease described by enzyme defects that further disturb glycogen synthesis and degradation cycle. In the present study, liver biopsy showed that all 40 cases were GSD. Local study done by Bilal H et al from Lahore Pakistan revealed that 79.7% children were having GSD type-1.[9] The literature has shown that GSD tyope-1 is the most common GSD while GSD type-III is known to be the second most frequent GSD globally.[4]

We found that 55.0% children with GSD were boys. The literature does not show certain inclination towards a specific gender in GSD[10] but a recent local study published from Ahmed S et al showed that 74.5% children with GSD were boys so our findings are pretty consistent with the local literture.[11] A study done by Moraru E et al found equal proportion of boys and girls among GSD type-1 children studied.[12] The mean age of our study cases was 2.8±1.7 years. Our findings are comparable with what was found by Bilal H et al where they noted mean age of children with GSD type-1 to be 2.09±1.65.[9] Usually, GSD is thought to exhibit in the infancy period and it commonly presents in the form of abdominal distension, hepatomegaly, short stature, doll's facies and recurrent diarrhea as has been reported in the literature.[13,14]

Abdominal distension and hepatomegaly and abdominal distention were the most common presentation reported in 100% children each and our findings are pretty consistent what has been reported in the literature.[9,13,14] Some of the rare clinical presentations include pancreatitis, renal calculi or hepatic nodules.[15,16] In the present study, one child presented with renal stones. Along with clinical findings, biochemical and laboratory findings are considered to be very helpful especially for identifying metabolic disorders like hypertriglyceridemia, hypercholesterolemia and hypoglycemia as many of the children with GSD may present asymptomatic.[14] In the present work, ALT 2 time above upper limit normal, hypertriglyceridemia and hyperuricemia were noted among 92.5%, 80.0% and 40.0% children respectively. Bilal H et al reported hypertriglyceridemia, hypercholesterolemia and hypoglycemia to be present in 92.9%, 63.3% and 14% children respectively.[9] Literature reports hyperuricemia to be present in about 20-30% children in the 1st decade of life while its risk increases more in the 2nd decade. In this study, hyperurecemia was reported in 40.0% children which is relatively high to what has been reported by others in the past.[4,9] Initiation of metabolic crises among children with GSD may start exhibiting in the form of hypoglycemia that can further progress into metabolic acidosis, convulsions and ultimately result in death if these conditions are not identified, addressed and managed timely. Liver biopsy is known to be the best method for labeling GSD especially in the developing countries but clinical and biochemical assessment can further prove helpful. In the developed world, access to enzymes essays and genetic studies has almost made liver biopsy obsolete.

The present study is one of the few local studies conducted among children with GSD so it adds to what little is known about this rare entity. We were unable to note treatment details and outcomes in the current set of patients. Further prospective trials are necessary to further enlighten us about the various insights of GSD.

CONCLUSION

Abdominal distension, hepatomegaly and increased appetite were the most common clinical presentation among children with GSD. Biochemical investigations revealed

that ALT 2 time above upper limit normal, hypertriglyceridemia and hyperuricemia were the most frequent among GSD children.

REFERENCES

1. Ellingwood SS, Cheng A. **Biochemical and clinical aspects of glycogen storage diseases.** J Endocrinol. 2018 Sep 1; 238(3):R131-R141.

2. Kilimann MW, Oldfors A. **Glycogen pathways in disease: New developments in a classical field of medical genetics.** J Inherit Metabol Dis. 2015; 38(3):483-487.

3. Chen MA, Weinstein DA. **Glycogen storage diseases: Diagnosis, treatment and outcome.** Translational Sci Rare Dis. 2016; 1(1):45-72.

4. Saeed A, Arshad H, Alvi A, Suleman H. **Clinical presentation and biochemical findings in children with glycogen storage disease type 1a.** Pak Armed Forces Med J. 2015; 65(5):682-685.

5. Lin CC, Tsai JD, Lin SP, Lee HC. **Renal sonographic findings of type I glycogen storage disease in infancy and early childhood.** Pediatr Radiol. 2005; 35(8):786-791.

6. Kishnani PS, Goldstein J, Austin SL, Arn P, Bachrach B, Bali DS, et al. **Diagnosis and management of glycogen storage diseases type VI and IX: A clinical practice resource of the American College of Medical Genetics and Genomics (ACMG).** Genetics Med 2019; 19:1.

7. Chou JY, Matern D, Mansfield BC, Chen YT. **Type I glycogen storage diseases: Disorders of the glucose-6-phosphatase complex.** Curr Mol Med 2002; 2:121-143.

8. Matern D, Starzl TE, Arnaout W, et al. **Liver transplantation for glycogen storage disease types I, III, and IV.** Eur J Pediatr 1999; 158(Suppl 2): S43-48.

9. Bilal H, Cheema HA, Fayyaz Z, Saeed A, Hamdani SSB. **Hepatic glycogenosis in children: Spectrum of presentation and diagnostic modalities.** J Ayub Med Coll Abbottabad. 2019; 31(3):368–371.

10. Saeed A, Hoogerland JA, Wessel H, Heegsma J, Derks TGJ, van der Veer E, et al. **Glycogen storage disease type 1a is associated with disturbed vitamin A metabolism and elevated serum retinol levels.** Hum Mol Genet. 2020; 29(2):264-273.

11. Ahmed S, Akbar F, Ali AJ, Afroze B. **Clinical, pathological and molecular spectrum of patients with glycogen storage diseases in Pakistan.** J Pediatr Endocrinol Metab. 2022; 35(3):373-385.

12. Moraru E, Cuvinciuc O, Antonesei L, Mihaila D, Bozomitu L, Rusu T, Stana B, Sacaci P, Luchian A, Bratu L, Popescu A, Mircan O, Moraru D. **Glycogen storage disease type I--between chronic ambulatory follow-up and pediatric emergency.** J Gastrointestin Liver Dis. 2007 Mar; 16(1):47-51.

13. Ozen H. **Glycogen storage diseases: New perspectives.** World J Gastroenterol. 2007 May 14; 13(18):2541-2553.

14. Hicks J, Wartchow E, Mierau G. **Glycogen storage diseases: A brief review and update on clinical features, genetic abnormalities, pathologic features, and treatment.** Ultrastruct Pathol. 2011 Oct; 35(5):183-196.

15. Bhattacharya K. **Dietary dilemmas in the management of glycogen storage disease type I.** J Inherit Metab Dis. 2011; 34(3):621-629.

16. Lee PJ, Dalton RN, Shah V, Hindmarsh PC, Leonard JV. **Glomerular and tubular function in glycogen storage disease.** Pediatr Nephrol1995; 9(6):705-710.

AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Sasui Anam	Data collection, Drafitng.	
2	Arit Parakash	Study concept, Data analysis, Proof reading.	
3	Aisha Merchant	Methodology, Discussion.	