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GLYCOGENOSES AND AGLYCOGENOSES, MUCOPOLYSACCHARIDOSES, GALACTOSEMIA AND FRUCTOSEMIA: ETIOLOGY, PATHOGENESIS, CLINICAL CONSEQUENCES, AND PREVENTION

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Abstract: Inherited disorders of carbohydrate metabolism represent a heterogeneous group of genetic diseases characterized by abnormalities in the synthesis, degradation, transport, or utilization of carbohydrates. Glycogen storage diseases (glycogenoses), aglycogenoses, mucopolysaccharidoses, galactosemia, and hereditary fructose intolerance are among the most clinically significant metabolic disorders affecting carbohydrate metabolism. These diseases arise from defects in specific enzymes responsible for glycogen metabolism, lysosomal degradation of glycosaminoglycans, or the metabolism of galactose and fructose. Accumulation of toxic metabolites and energy deficiency lead to multisystem manifestations involving the liver, muscles, nervous system, heart, kidneys, and skeletal tissues. Advances in molecular genetics and newborn screening have significantly improved early diagnosis and patient outcomes. This review summarizes the biochemical basis, genetic mechanisms, clinical manifestations, complications, diagnostic approaches, and preventive strategies associated with these disorders. Understanding these inherited metabolic diseases is essential for improving therapeutic interventions and reducing disease-related morbidity and mortality.

Keywords: glycogenosis, aglycogenosis, mucopolysaccharidosis, galactosemia, fructosemia, inherited metabolic disorders, glycogen metabolism, prevention.

Introduction

Carbohydrate metabolism plays a fundamental role in maintaining cellular energy homeostasis and physiological function. Glucose, glycogen, galactose, fructose, and complex polysaccharides participate in numerous metabolic pathways that support growth, development, and tissue maintenance. Genetic defects affecting enzymes involved in these pathways result in inherited metabolic disorders characterized by substrate accumulation, toxic metabolite production, or impaired energy generation.[1,2,3,4,5,6]

Among the most important hereditary disorders of carbohydrate metabolism are glycogen storage diseases, glycogen synthase deficiencies (aglycogenoses), mucopolysaccharidoses, galactosemia, and hereditary fructose intolerance. Although individually rare, collectively these disorders contribute significantly to pediatric morbidity and mortality worldwide.[7,8,9,10,11]

The development of molecular diagnostics and expanded newborn screening programs has greatly improved disease detection and management. Nevertheless, early recognition remains critical for preventing irreversible organ damage and improving quality of life.[12,13,14,15,16]

Glycogen Metabolism and Its Physiological Importance

Glycogen serves as the primary storage form of glucose in animals. It is predominantly stored in:

- Liver
- Skeletal muscles
- Cardiac muscle

The liver maintains blood glucose levels during fasting, while muscle glycogen provides energy during physical activity.

Glycogen metabolism consists of two opposing processes:

Glycogenesis

The synthesis of glycogen from glucose.

Glycogenolysis

The breakdown of glycogen into glucose-1-phosphate and free glucose.

These pathways are tightly regulated by hormones, including insulin, glucagon, and epinephrine.[17,18,19,20,21]

Glycogen Storage Diseases (Glycogenoses)

Glycogen storage diseases (GSDs) comprise a group of inherited disorders caused by deficiencies of enzymes involved in glycogen metabolism.

More than fifteen types have been identified.

Type I Glycogenosis (Von Gierke Disease)

Enzyme Deficiency

Glucose-6-phosphatase deficiency.

Pathogenesis

Inability to convert glucose-6-phosphate into free glucose results in excessive glycogen accumulation within hepatocytes and renal cells.

Clinical Features

- Severe fasting hypoglycemia
- Hepatomegaly
- Growth retardation
- Hyperuricemia
- Hyperlipidemia
- Lactic acidosis

Long-Term Consequences

Untreated patients may develop hepatic adenomas and renal dysfunction.

Type II Glycogenosis (Pompe Disease)

Enzyme Deficiency

Lysosomal acid alpha-glucosidase deficiency.

Clinical Manifestations

- Cardiomyopathy
- Progressive muscle weakness
- Respiratory insufficiency

Outcome

Infantile forms often lead to early mortality without treatment.

Type III Glycogenosis (Cori Disease)

Caused by deficiency of the glycogen debranching enzyme.

Clinical manifestations include:

- Hepatomegaly
- Muscle weakness
- Growth delay
- Hypoglycemia

Type V Glycogenosis (McArdle Disease)

Deficiency of muscle glycogen phosphorylase.

Symptoms include:

- Exercise intolerance
- Muscle cramps
- Myoglobinuria
- Fatigue

Aglycogenoses

Aglycogenosis refers to disorders characterized by inadequate glycogen synthesis.

The most common form results from glycogen synthase deficiency.[22,23,24,25,26]

Biochemical Consequences

The inability to synthesize glycogen leads to:

- Reduced glucose storage capacity
- Fasting hypoglycemia
- Ketosis
- Neurological manifestations

Clinical Presentation

Patients may develop:

- Seizures
- Developmental delay
- Exercise intolerance
- Episodic hypoglycemia

Because glycogen reserves are absent or severely reduced, energy supply during fasting becomes critically compromised.[27,28,29]

Mucopolysaccharidoses

Mucopolysaccharidoses (MPS) are lysosomal storage diseases caused by deficiencies of enzymes responsible for degrading glycosaminoglycans (GAGs).

Incomplete degradation leads to progressive accumulation of GAGs within lysosomes.[30,31,32,33]

Affected tissues include:

- Bone
- Cartilage
- Heart
- Liver
- Spleen

- Central nervous system

Classification of Mucopolysaccharidoses

Several major forms have been identified.

MPS I (Hurler Syndrome)

Enzyme Deficiency

Alpha-L-iduronidase.

Clinical Features

- Coarse facial features
- Developmental delay
- Corneal clouding
- Skeletal abnormalities
- Hepatosplenomegaly

MPS II (Hunter Syndrome)

Enzyme Deficiency

Iduronate-2-sulfatase.

Characteristics

- Similar to Hurler syndrome
- X-linked inheritance
- Absence of corneal clouding

MPS III (Sanfilippo Syndrome)

Primarily affects the nervous system.

Clinical manifestations include:

- Progressive neurodegeneration
- Behavioral disturbances
- Cognitive decline

MPS IV (Morquio Syndrome)

Characterized by severe skeletal abnormalities with relatively preserved intellectual development.

MPS VI (Maroteaux-Lamy Syndrome)

Associated with:

- Skeletal deformities
- Cardiac involvement
- Growth retardation

Intellectual function is usually preserved.

Galactosemia

Galactosemia is an inherited disorder resulting from defects in galactose metabolism.[34,35,36]

Biochemical Basis

The most common form results from deficiency of:

Galactose-1-phosphate uridyltransferase (GALT)

This deficiency leads to accumulation of toxic metabolites including galactose-1-phosphate.

Clinical Manifestations

Symptoms often appear shortly after milk feeding begins.

Common findings include:

- Vomiting
- Jaundice
- Hepatomegaly
- Cataracts
- Failure to thrive
- Developmental delay

Severe cases may progress to liver failure and sepsis.

Long-Term Consequences

Despite treatment, some patients may develop:

- Speech disorders
- Learning difficulties
- Ovarian insufficiency
- Neurological complications

Fructosemia and Hereditary Fructose Intolerance

Hereditary fructose intolerance results from deficiency of aldolase B.

Pathogenesis

Accumulation of fructose-1-phosphate causes:

- ATP depletion
- Hepatic toxicity
- Renal dysfunction

Clinical Manifestations

Symptoms appear after introduction of fructose-containing foods.

Patients commonly develop:

- Nausea
- Vomiting
- Hypoglycemia
- Hepatomegaly
- Growth failure

Untreated disease may progress to severe liver damage.

Diagnostic Approaches

Modern diagnosis relies upon multiple methods.

Biochemical Testing

Includes measurement of:

- Blood glucose
- Lactate
- Liver enzymes
- Metabolic intermediates

Enzyme Activity Assays

Direct determination of enzyme function remains a cornerstone of diagnosis.

Molecular Genetic Testing

Identification of pathogenic mutations allows:

- Confirmation of diagnosis
- Carrier detection
- Prenatal diagnosis
- Genetic counseling

Newborn Screening

Early detection significantly improves clinical outcomes.

Prevention Strategies

Genetic Counseling

Families with known mutations should receive professional genetic counseling.

Benefits include:

- Risk assessment
- Prenatal diagnosis
- Reproductive planning

Newborn Screening Programs

Screening permits:

- Early intervention
- Prevention of irreversible complications
- Improved survival

Dietary Management

Diet remains the primary preventive strategy for many disorders.

Galactosemia

Strict elimination of galactose-containing foods.

Hereditary Fructose Intolerance

Avoidance of fructose, sucrose, and sorbitol.

Glycogenoses

Frequent meals and cornstarch therapy help prevent hypoglycemia.

Enzyme Replacement Therapy

Available for several lysosomal storage diseases including:

- Pompe disease
- Hurler syndrome
- Hunter syndrome
- Maroteaux-Lamy syndrome

These therapies improve quality of life and reduce disease progression.

Public Health Measures

Prevention should include:

- Expanded newborn screening
- Prenatal diagnostics
- Public awareness campaigns
- Access to specialized metabolic centers

Future Perspectives

Advances in biotechnology continue to transform management of inherited metabolic diseases.

Emerging approaches include:

- Gene therapy
- Genome editing
- Stem cell transplantation
- Personalized medicine
- RNA-based therapeutics

These innovations offer promising opportunities for curative treatment.

Conclusion

Glycogenoses, aglycogenoses, mucopolysaccharidoses, galactosemia, and hereditary fructose intolerance represent important inherited disorders of carbohydrate metabolism. These diseases arise from specific enzymatic defects that disrupt normal metabolic pathways and lead to toxic metabolite accumulation or impaired energy production. Early diagnosis through newborn screening and molecular testing is essential for preventing irreversible organ damage. Advances in enzyme replacement therapy, dietary management, and genetic technologies have significantly improved prognosis. Continued research into molecular mechanisms and innovative treatments is expected to further enhance outcomes for affected individuals.

REFERENCES:

1.Chen YT. Glycogen Storage Diseases. In: The Metabolic and Molecular Bases of Inherited Disease.

2.Kishnani PS, et al. Pompe Disease Diagnosis and Management Guidelines. Genetics in Medicine. 2016.

3.Bali DS, et al. Glycogen Storage Disease Type I. GeneReviews. 2023.

4.Weinstein DA, et al. Glycogen Storage Diseases. Clinical Liver Disease. 2018.

5.Neufeld EF, Muenzer J. The Mucopolysaccharidoses. In: The Metabolic and Molecular Bases of Inherited Disease.

6.Makhamatov, U., Malikov, N., Po‘latov, S., Yusupov, M., Ibragimov, U., Kenjayeva, X., & Umarov, S. (2026). ORGANIZING HEALTHY AND SAFE NUTRITION IN NON-COMMUNICABLE DISEASES. *Shokh Articles Library*, *1*(1).

7.SOG‘LOM TURMUSH TARZINI TASHKIL ETISHNI DOLZARB MUAMMOLARI VA ULARNING YECHIMLARI. M .Ashurova, U Maxamatov, X Xaitov, S Yakubov, U Ibragimov. SCIENTIFIC ASPECTS AND TRENDS IN THE FIELD OF SCIENTIFIC RESEARCH 3 (33), 57-61

8. Flatulence in Children and Adolescents and its Prevention. U Shoirjonovich, KM Abdulkhamidovna. European Journal of Innovation in Nonformal Education 2 (1), 83-85

9. Its Importance for The Health of the Child and Mother. HA Akhunjonova, US Makhamatov, KM Saydullayeva, KO Khojimatov, ...Journal of clinical and preventive medicine 2, 61-64

10. HISTOSTRUCTURE OF THE GASTRIC MUCOUS MEMBRANE OF RATS WITH A SINGLE PROTEIN DIET. S Salomov, XM Aliyev, PP Rakhmanov, MD Ashurova, US Makhamatov. EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE 2 (4), 14-16
11. Platelet deficiency disease among children and adolescents and measures to prevent it. KMA Makhamatov U.Sh. Eurasian Medical Research Periodical, 37-39
12. Food Poisoning and Its Prevention and Disposal Methods. XU Baxodirovna, MU Shoirjonovich. Мировая наука, 85-87
13. Negative Consequences of Poor and Irregular Diet and Recommendations for Healthy Diet. MD Ashurova, US Maxamatov, UA Teshaboyev, KM Saydullayeva
Ethiopian International Journal of Multidisciplinary Research 10 (11), 509-512
14. Integral Helmintoses in Children and Their Etiological Factors. U Maxamatov, M Xabibullayeva. IQRO JURNALI 1 (2), 233-236
15. CLINIC, DIAGNOSIS OF BOTULISM IN CHILDREN AND ADOLESCENTS OF SCHOOL AGE MUS COURSE. World Bulletin of Public Health 18, 50-52
16. Nutrition of Young Mothers and Recommendations. U Maxamatov, A Nematullayev, D Raimjonov, J Ikromov. Eurasian Journal of Medical and Natural Sciences 2 (6), 160-162
17. Negative Consequences of More Eating and Recommendations on Eating
U Maxamatov, D Raimjonov, J Ikromov, A Nematullayev
Евразийский журнал медицинских и естественных наук 2 (6), 156-159
18. THE EFFECTIVENESS OF URGENT MEDICAL INSTRUCTIONS IN EMERGENCY STATIONS. MU Shoirjonovich, XU Baxodirovna
Мировая наука, 37-40
19. Determining the health of children and adolescents. M.D. Ashurova, U.Sh. Makhamatov, K.M. Saydullaeva, A.L Valiyev, F.I Isroilov. BIO Web of Conferences 65, 05029
20. THE PLACE AND ROLE OF HEALTHY AND HIGH-QUALITY NUTRITION IN STUDENTS'MASTERY OF EDUCATIONAL ACTIVITIES
MD Ashurova. Ethiopian International Journal of Multidisciplinary Research 10 (11), 506-508
21. Anemia Disease and Rational Nutrition in it. U Makhamatov IQRO 2 (2), 280-283
22. Gigenic Bases of Optimization of Children and Comments Nursed in General Schools. U Maxamatov. Web of Semantic: Universal Journal on Innovative Education 2 (3), 56-65
23. Treatment of Triggeral Helmintosis in Children and Adolescents Using Folk Medicine. U.Sh. Maxamatov. Univer Publishing
24. Анализ пациентов с инфекцией COVID-19, роль микроэлемента цинка в организме человека и его роль в распространении и профилактике заболевания. УА Тешабоев, ХК Рузматова, УШ Махаматов, КМ Сайдуллаева
Экономика и социум, 374-381
25. Vitamins and Human health. UB Xatamova, US Maxamatov. Мировая наука, 83-85

26. OPTIMAL NUTRITION PROGRAM FOR CHILDREN: DEVELOPMENT AND IMPLEMENTATION. M Umidjon Modern World Education: New Age Problems–New solutions 1 (3), 70-72

27. ОЖИРЕНИЕ И ЕГО ПОСЛЕДСТВИЯ. У Махаматов Научный Импульс 3 (26), 69-73

28. EKSTRAGENITAL PATOLOGIYALAR, HOMILADORLIKNING O‘ZARO BIR BIRIGA TA'SIRI VA BU HOLATDA OVQATLANISH TARTIBI
U Maxamatov, D Abselyamov, X Kenjayeva, S Po‘latov. MASTERS 3 (3), 5-10

29. CARDIOVASCULAR DISEASES AND HYGIENIC PRINCIPLES OF HEALTHY NUTRITION. F Mamadaliyev, D Abselyamov, S Pulatov, K Kenjayeva, U Maxamatov. Journal of Multidisciplinary Sciences and Innovations 1 (2), 765-768

30. EMERGENCY SITUATIONS RESPONSIBILITIES AND PREVENTION MEASURES. MU Shoirjonovich, XU Baxodirovna. Мировая наука, 33-36

31. РАЗВИТИЕ ДИАБЕТА У БОЛЬНЫХ ИНФЕКЦИЕЙ COVID-19//Евразийский журнал медицинских и естественных наук.–2022
УШ Махаматов. Т 2 (5), 13-18

32. СТАНОВЛЕНИЕ МИКРОБИОЦЕНОЗА У НЕДОНОШЕННЫХ И НОРМАЛЬНОРОЖДЁННЫХ НОВОРОЖДЕННЫХ ДЕТЕЙ
РМ Шерматов, УШ Махаматов. Актуальные научные исследования в современном мире, 76-79

33. METABOLISM OF BASIC SUBSTANCES AND THEIR SIGNIFICANCE IN THE BODY. U Maxamatov, D Abselyamov. MODELS AND METHODS FOR INCREASING THE EFFICIENCY OF INNOVATIVE RESEARCH 4

34. Makhamatov U., Muslimakhon R. THE ROLE OF UNHEALTHY DIET IN THE PATHOGENESIS OF NON-COMMUNICABLE DISEASES //AMERICAN JOURNAL OF APPLIED MEDICAL SCIENCE. – 2025. – Т. 3. – №. 10. – С. 63-72.

35. Makhamatov U., Muslimakhon R. NUTRITION OPTIMIZATION IN OSTEOPOROSIS FOLLOWING COVID-19 //AMERICAN JOURNAL OF APPLIED MEDICAL SCIENCE. – 2025. – Т. 3. – №. 10. – С. 52-62.

36. Maxamatov U., Muslimaxon R. SOG'LOM TURMUSH TARZI SALOMATLIK OMILI //AMERICAN JOURNAL OF APPLIED MEDICAL SCIENCE. – 2025. – Т. 3. – №. 10. – С. 73-82.