

Wolcott–Rallison Syndrome: Raising Awareness Today for Better Care Tomorrow – A Case Report

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ABSTRACT

Wolcott–Rallison syndrome is a rare inherited disorder characterized mainly by permanent neonatal diabetes mellitus and multisystem complications. It is commonly associated with mutations in the Eif2AK3 gene and is inherited in an autosomal recessive manner. A 2-year-old male child presented with poor feeding, excessive thirst, frequent urination, recurrent fever, vomiting, poor weight gain, and dehydration. Investigations revealed persistent hyperglycemia, elevated liver enzymes, and features suggestive of skeletal abnormalities. The child was managed with insulin therapy, fluid and electrolyte management, nutritional support, monitoring of liver function, and supportive care. Nursing management focused on blood glucose monitoring, hydration, nutrition, prevention of complications, growth monitoring, medication administration, and parental education. Early diagnosis and multidisciplinary management are important to improve outcomes and quality of life in children with Wolcott–Rallison syndrome.

Keywords: inherited autosomal recessive disorder, skeletal abnormalities, multisystem complications

Case scenario: A 2-year-old male child is brought to the pediatric department with recurrent episodes of fever, poor feeding, vomiting, and excessive thirst. The child was diagnosed with permanent neonatal diabetes mellitus during infancy and requires insulin therapy. On examination, the child has low body weight and signs of dehydration. Laboratory investigations reveal hyperglycemia and elevated liver enzymes. Genetic evaluation is suggestive of Wolcott–Rallison syndrome. The child is admitted for stabilization, glucose control, hydration, and further evaluation.

INTRODUCTION:

Wolcott–Rallison syndrome (WRS) is a rare inherited disorder characterized mainly by permanent neonatal diabetes mellitus associated with skeletal abnormalities and episodes of acute liver dysfunction. It is usually caused by mutations in the EIF2AK3 gene and follows an autosomal recessive pattern of inheritance. Children with WRS may develop diabetes during the first months of life and may later develop recurrent episodes of liver dysfunction, skeletal abnormalities, growth retardation, and other complications. Early diagnosis, insulin therapy, monitoring of blood glu-

cose, nutritional support, and management of complications are important for improving the child's health.¹

Literature review:

Julier and Nicolino published a review article on Wolcott–Rallison syndrome in the Orphanet Journal of Rare Diseases. They described it as a rare autosomal recessive disorder characterized by permanent neonatal diabetes mellitus, skeletal dysplasia, and growth retardation. The authors explained that mutations in the EIF2AK3 gene are responsible for the disorder. They also highlighted the importance of early diagnosis, insulin therapy, monitoring of liver function, and genetic counselling.

Memon et al. (2022) Memon and colleagues reported three patients with Wolcott–Rallison syndrome in Pediatric Endocrinology, Diabetes and Metabolism. The patients presented with early-onset diabetes, and genetic testing identified EIF2AK3 mutations. The study highlighted the importance of genetic testing in children who develop diabetes during the first six months of life. The authors also emphasized regular monitoring for liver dysfunction and other complications.

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Aldrian et al. (2024) Aldrian and colleagues published a systematic review and follow-up study on Wolcott–Rallison syndrome in Liver International. Their study reviewed the clinical features and complications of the disorder, including neonatal diabetes, liver dysfunction, growth impairment, and skeletal abnormalities. The findings demonstrated that the condition can affect multiple organs and that the severity varies among patients. The authors emphasized early recognition, regular follow-up, and multidisciplinary management.^{2,6}

Definition:

Wolcott–Rallison syndrome is a rare autosomal recessive genetic disorder characterized primarily by permanent neonatal diabetes mellitus, with additional features such as skeletal abnormalities, growth retardation, and recurrent episodes of liver dysfunction.^{1,6}

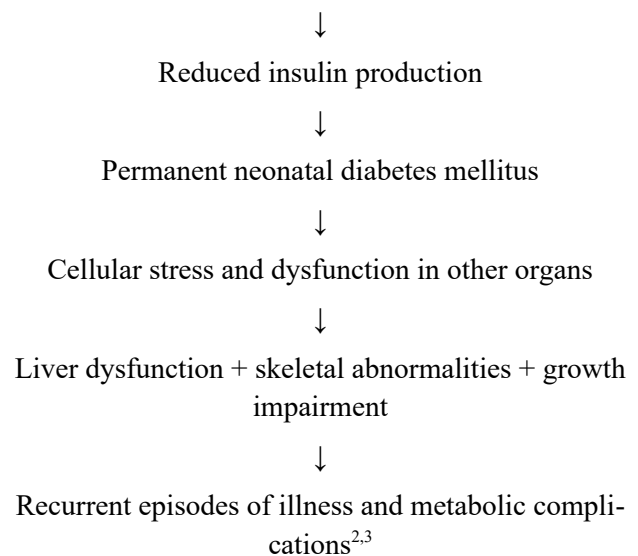
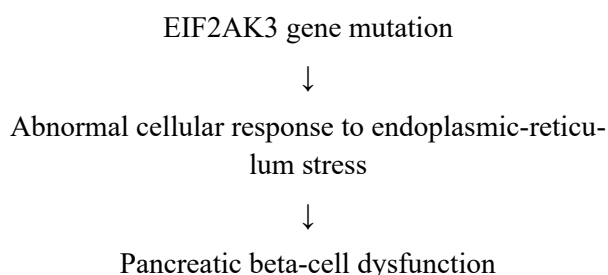
Etiology and Risk factor :

The major cause of Wolcott–Rallison syndrome is a pathogenic mutation in the **EIF2AK3** gene. The **EIF2AK3** gene produces a protein involved in the cellular response to endoplasmic-reticulum stress. Dysfunction of this pathway particularly affects pancreatic beta cells and other tissues Inheritance. Autosomal recessive inheritance. Both parents are usually carriers of the abnormal gene. The disorder can occur when a child inherits an abnormal copy of the gene from both parents.

Possible risk factors include:

- Family history of Wolcott–Rallison syndrome
- Consanguineous marriage
- Parents carrying pathogenic EIF2AK3 variants
- Previous child affected by neonatal diabetes associated with WRS
- Family history of unexplained neonatal diabetes or early childhood liver dysfunction^{3,6}

Pathophysiology:



Clinical Manifestation:

- Permanent neonatal diabetes mellitus
- Hyperglycemia
- Excessive thirst
- Frequent urination
- Poor weight gain
- Growth retardation
- Recurrent fever
- Vomiting
- Dehydration
- Episodes of acute liver dysfunction
- Elevated liver enzymes
- Skeletal abnormalities
- Osteopenia or other bone abnormalities
- Muscle weakness^{3,4}

Diagnostic Evaluation :

A. Blood investigations

- Blood glucose
- HbA1c
- Serum electrolytes
- Liver function tests
- Renal function tests
- Complete blood count

B. Diabetes-related investigations

- Fasting/random blood glucose

- Urine glucose
- Urine ketones when indicated
- C-peptide assessment where appropriate

C. Imaging

- X-ray of bones when skeletal abnormalities are suspected
- Abdominal ultrasound for assessment of liver and other abdominal organs

D. Genetic testing

- Genetic testing can identify pathogenic variants in the EIF2AK3 gene and help confirm the diagnosis

Medical Management:

A. Insulin therapy

- Regular insulin administration as prescribed
- Frequent monitoring of blood glucose
- Adjustment of insulin according to glucose levels, nutrition, and illness

B. Fluid and electrolyte management

- Assess hydration status
- Provide oral or IV fluids as prescribed
- Monitor electrolytes

C. Management of liver dysfunction

- Regular liver function monitoring
- Identify and treat precipitating factors
- Supportive management during acute episodes

D. Nutritional management

- Adequate calories and protein
- Age-appropriate diet
- Monitor weight and growth
- Dietary planning according to insulin therapy

E. Management of skeletal abnormalities

- Monitor bone health
- Adequate calcium and vitamin D when prescribed
- Physiotherapy where required.^{1,4,5}

Nursing Management:

I. Assessment

- Monitor vital signs.
- Monitor blood glucose regularly.
- Assess hydration status.
- Monitor intake and output.
- Assess nutritional status.
- Record daily/regular weight.
- Observe for signs of hypoglycemia and hyperglycemia.
- Monitor for vomiting and fever.
- Observe for signs of liver dysfunction.
- Assess physical growth and development.
- Assess mobility and skeletal abnormalities.
- Monitor laboratory investigations.

II. Nursing interventions

- Administer insulin as prescribed.
- Monitor blood glucose before meals and as ordered.
- Observe for symptoms of hypoglycemia.
- Encourage adequate fluid intake when appropriate.
- Maintain accurate intake and output records.
- Provide prescribed nutritional support.
- Monitor weight and growth.
- Administer medications as prescribed.
- Maintain infection-control measures.
- Provide comfort during episodes of fever or illness.
- Monitor liver function results.
- Encourage appropriate physical activity according to the child's condition.
- Maintain a safe environment to prevent injury.
- Provide emotional support to the child and parents

Nursing Diagnosis:

- 1) Risk for unstable blood glucose level related to impaired insulin production.
- 2) Deficient fluid volume related to increased urinary fluid loss secondary to hyperglycemia.

- 3) Imbalanced nutrition: less than body requirements related to metabolic abnormalities and inadequate intake.
- 4) Delayed growth and development related to chronic metabolic disorder.
- 5) Risk for injury related to hypoglycemic episodes and skeletal abnormalities.
- 6) Anxiety of parents related to the child's chronic genetic condition and long-term treatment requirements.⁵

Nursing Care Plan

Nursing diagnosis	Goals/ Expected outcomes	Nursing Intervention	Rationale	Evaluation
Risk for unstable blood glucose level	Child will maintain blood glucose within prescribed target range.	Monitor glucose; Administer insulin; Observe for hypo/hyperglycemia	Helps maintain glucose control and prevent complications	Blood glucose improves
Risk for unstable blood glucose level	Child will maintain adequate hydration improves	Monitor I/O Mucous membranes, urine output provide fluids as prescribed	Prevents dehydration and electrolyte imbalance	Hydration improves
Imbalanced nutrition: less than body requirements	Child will achieve adequate Nutritional intake & weight gain	Monitor weight; Provide small frequent meals; Collaborate with dietitian	Supports growth and metabolic needs	Weight and intake improve
Delayed growth and development	Child will show appropriate developmental progress	Monitor height/weight; Encourage developmental activities; Refer when needed	Early intervention supports development	Development monitored
Anxiety of parents	Parents will verbalize reduced anxiety and understanding	Provide information; Allow questions; Provide emotional support; explain treatment	Knowledge improves coping and confidence	Parents demonstrate understanding

CONCLUSION:

Wolcott–Rallison syndrome is a rare inherited disorder characterized mainly by permanent neonatal diabetes mellitus with multisystem complications. Early identification of the condition is important for appropriate management. Nursing care focuses on maintaining blood glucose, hydration, nutrition, growth, safety, and early recognition of complications. Proper parent education and multidisciplinary follow-up are essential for long-term care.^{1,4,6}

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