

Editorial

Nutrition as Precision Therapy in Rare Genetic Diseases: Moving beyond Supportive Care in The Era of Genomics and Global Inequity

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Rare diseases affect over 300 million individuals worldwide, creating a significant but often overlooked public health issue. Approximately 70 to 80 percent of these conditions are genetic, often causing disruptions in metabolic pathways that relate directly to how our bodies process and use nutrients. In this context, nutrition is not just a supportive element of care; it is increasingly becoming an essential, mechanism-driven treatment approach.

In the past decade, advances in genomics, metabolomics, and systems biology have significantly changed our understanding of rare diseases. These conditions have shifted from being clinically diverse to being more biochemically understandable, many of which can be addressed with targeted dietary changes. This change not only affects clinical practices but also impacts health systems, especially in low- and middle-income countries like India, where access to sophisticated therapies is often limited.

From Metabolic Defect to Nutritional Target

Many rare genetic diseases stem from a disruption in the enzymatic pathways critical for nutrient metabolism. These defects can result in: Accumulation of toxic substrates, Deficiency of essential metabolites, Impaired energy production.

Dietary intervention acts to correct these issues by either limiting harmful substances, supplying missing compounds, or bypassing metabolic obstacles. A classic case is phenylketonuria (PKU), where limiting phenylalanine in the diet stops irreversible

brain damage. This example clearly shows the link between genes, diet, and health outcomes, underscoring how nutrition can serve as a therapy that alters disease progression.¹

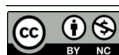
Beyond PKU, similar principles apply to various inborn errors of metabolism (IEMs), including urea cycle disorders and organic acidemias, where adjusting dietary protein helps prevent harmful metabolite build-up.²

Nutrition in Rare Neurological and Multisystem Disorders

Recent studies have broadened the role of nutritional therapy beyond traditional metabolic disorders. A 2024 review looked at dietary interventions in rare neurological diseases and found that nutrition can modify disease, serve as an additional therapy, and in some cases, act as the primary treatment.

This review combined data from laboratory and clinical studies on various genetic conditions, such as leukodystrophies, rare epilepsies, and neurodevelopmental syndromes, showing that dietary factors can influence when diseases start, how they progress, and the intensity of symptoms.

Notably, diets like the ketogenic diet have shown success in conditions such as GLUT1 deficiency and pyruvate dehydrogenase deficiency, providing ketones as an alternative energy source for the brain. However, the evidence is limited due to small sample sizes and variability in how studies are designed.



The Rise of Medical Nutrition Therapy

A significant change in this field is moving from focusing on single nutrients to using structured dietary systems, including foods for special medical purposes (FSMPs). These products are specifically designed to meet the metabolic needs of patients with rare diseases, and they are becoming an important part of therapy.

Recent research highlights how FSMPs can provide specialized nutritional formulas tailored to specific diseases, allowing for better metabolic regulation. This shift signifies a new understanding: nutrition is now seen as a vital part of treatment alongside drugs, genetic therapies, and dietary strategies.

Nutrigenomics and Precision Nutrition

The rise of nutrigenomics has further supported the scientific basis for dietary strategies in rare diseases. By combining genomic, transcriptomic, metabolomic, and microbiome data, researchers are starting to understand how genetic variations affect dietary responses.³

Research from 2025 shows that combining genetic and metabolic profiling can lead to highly personalized dietary recommendations that target specific molecular issues. Similarly, recent reviews emphasize that dietary therapies can be tailored to address metabolic problems in individuals, marking progress towards more personalized medicine.³

Rare diseases offer a strong foundation for this approach because their single-gene origins make gene-diet interactions easier to understand compared to complex, polygenic conditions.

OPPORTUNITY AMID CONSTRAINTS

India is a key area for applying nutrition-focused treatments for rare diseases. With a large population, unique genetic diversity, and growing acknowledgment of rare diseases in national health policies, the country faces both challenges and opportunities.

The National Policy for Rare Diseases (NPRD) 2021 recognizes the importance of diet management in metabolic disorders and supports financial assistance for treatments, including nutritional therapies. However, implementation is inconsistent due to:

- Limited availability of specialized medical foods
- High costs of long-term dietary treatments
- Shortage of trained metabolic dietitians
- Inadequate newborn screening programs

In many instances, especially in resource-poor settings, dietary intervention may be the only viable treatment since advanced therapies like enzyme replacement or gene therapies are often too costly.

India's Centers of Excellence (CoEs), such as AIIMS, provide an opportunity to connect clinical care, research, and nutritional strategies. However, expanding these models to broader health systems is a challenge.

Equity, Access, and the Global Nutrition Gap

Although nutrition-based therapies are often positioned as cost-effective alternatives to pharmacological treatments, their real-world accessibility remains uneven. Even in high-income settings, adherence to medically prescribed diets can be difficult to sustain due to social pressures, economic constraints, and the complexity of long-term dietary modifications. These challenges are amplified in low- and middle-income countries, where systemic barriers further restrict access.

Globally, disparities in access to therapeutic nutrition are pronounced. Specialised diets and medical foods, which are essential for managing many rare metabolic disorders, are frequently either unavailable or prohibitively expensive. In addition, culturally embedded dietary practices may conflict with restrictive or highly specific nutritional regimens, making adherence both socially and practically challenging. Health systems in many regions are also not adequately equipped to support long-term dietary monitoring, lacking trained personnel such as metabolic dietitians and structured follow-up mechanisms.⁴

These factors collectively highlight a fundamental paradox: while nutrition is theoretically one of the most accessible and non-invasive therapeutic options, it is often among the most difficult to implement effectively at scale. Bridging this gap requires not only scientific innovation but also health system strengthening, policy support, and culturally sensitive intervention models.

Despite a strong mechanistic foundation and clear clinical success in select conditions, the evidence supporting nutritional interventions in rare diseases is subject to several important limitations. One of the primary challenges is the inherently small and heterogeneous patient populations associated with rare diseases. This makes it difficult to conduct large, statistically robust clinical trials and limits the generalisability of findings.

Furthermore, there is a notable scarcity of well-designed randomized controlled trials in this field. Much of the existing evidence is derived from observational studies, case series, and expert consensus, which, while valuable, do not provide the same level of causal certainty as controlled trials. This limitation is compounded by a frequent reliance on surrogate biochemical markers, such as metabolite levels, rather than clinically meaningful outcomes like functional status, neurodevelopment, or quality of life.

CONCLUSION

Rare genetic diseases clearly show how nutrition can act as a precise, mechanism-based treatment rather than just a supportive measure. The convergence of genomics, metabolomics, and nutritional science is

changing the way we view diet as a targeted therapy that aligns with the principles of personalized medicine. Realizing this potential depends on addressing key gaps in evidence, access, and implementation. In countries like India, where there are limited resources for advanced treatments, nutrition-based interventions offer a scalable and impactful solution. The future of managing rare diseases will not rely only on gene therapy or medication innovations. It will depend on our ability to combine biology, nutrition, and healthcare systems into a coherent and fair model of care.

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