v. 5, n. 2, 2025

International Journal of Health Science

Acceptance date: 06/01/2025

DIET AND NUTRITION IN RETT SYNDROME: A LITERATURE REVIEW

Julia Cardoso Jerônimo
Centro Multidisciplinar UFRJ-Macaé, Rio de Janeiro, Brasil, Macaé, RJ
http://lattes.cnpq.br/0869743597558503

Renata Borba de Amorim Oliveira
Centro Multidisciplinar UFRJ-Macaé, Rio de Janeiro, Brasil, Macaé, RJ
http://lattes.cnpq.br/4871566247678443

Abstract: Rett syndrome is a rare genetic neurological disorder that predominantly affects girls, characterized by a progressive regression of motor and cognitive skills, accompanied by a series of severe symptoms, including gastrointestinal problems and eating difficulties. These challenges make patient nutrition an area of high relevance in the context of complementary treatments. This paper aims to carry out a literature review on the influence of diet and nutrition on the quality of life of patients with Rett Syndrome, exploring nutritional practices and interventions that can mitigate the symptoms of the condition and promote general well-being. Thus, the review covers scientific studies published in the last 12 years, which address diet, quality of life in patients with Rett Syndrome and recommendations for adapted nutritional intervention, also discussing the difficulties faced by caregivers in implementing these practices. The research was carried out using various databases, including the *National Library of Medicine* (Pubmed), *Scientific Electronic Library Online* (SCIELO), *Latin American and Caribbean Literature in Health Sciences* (LILACS) and *Periódicos Capes,* in English, Portuguese and Spanish. The following keywords were used: "Rett syndrome", "Rett syndrome and nutrition", "Quality of life", "Adequate nutrition", "Epilepsy", "Gastrointestinal problems", "Nutritional therapy" and "Multidisciplinary treatment". The results show that adequate nutrition can play a fundamental role in relieving symptoms such as irritability, seizures, swallowing problems and improving general condition. Based on the evidence analyzed, this research proposes personalized nutritional guidelines that can help health professionals and family members build dietary strategies that respect the individual needs of each patient. However, by synthesizing the advances and gaps in knowledge about nutrition in Rett syndrome, this study reinforces the importance of nutrition as a central component in therapeutic support and quality of life for these patients.

INTRODUCTION

Rett Syndrome (RS) is a complex and rare neurological disorder that stands out for the severity of its symptoms and the devastating impact on child development. Affecting girls mainly due to its genetic origin linked to the X chromosome, it was first described in the 1960s by neurologist Andreas Rett. Its course is marked by a characteristic pattern of apparently normal initial development, followed by a rapid and significant regression in motor and cognitive skills, which usually manifests itself between the ages of six months and two years (Arancibia et al., 2023).

Alterations in the MECP2 gene, located on the X chromosome, are known to be the primary cause of Rett syndrome. This gene plays a crucial role in the regulation of other genes and in the development and maintenance of the central nervous system. Dysfunction of the MECP2 gene therefore leads to a series of profound neurological and behavioral symptoms, which include motor disorders, communication difficulties, epileptic seizures, respiratory problems and, especially, nutritional complications (Kyle et al., 2018).

Among the many challenges of Rett syndrome, dietary and nutritional issues stand out due to their complexity and direct impact on patients' health and quality of life. Swallowing difficulties, frequent gastrointestinal problems, low weight and specific nutritional demands are common features of this condition and represent significant obstacles to maintaining an adequate nutritional status (Fu et al., 2020). Spasticity and other motor problems, such as involuntary movements and low muscle mass, also influence basal energy expenditure, contributing to increased nutritional needs. These factors, as well as bone

vulnerability, are widely observed in patients with SR, which increase the risk of osteoporosis and fractures, often requiring supplementation of micronutrients such as calcium and vitamin D (Motil et al., 2012).

Nutrition and diet therefore play an essential and complex role in Rett Syndrome, and are seen as fundamental therapeutic components for these patients. However, the topic is still insufficiently explored in the scientific literature, reflecting a lack of data for specific clinical guidelines or studies investigating nutritional practices, especially in relation to the individualization of strategies according to the progression and variability of the syndrome. This gap makes it difficult to standardize approaches for health professionals, family members and caregivers, who are faced with a series of challenges when trying to promote a safe and comfortable eating environment for the patient, as well as ensuring nutrition that meets individual needs.

Given this context, there is a pressing need for more studies to address aspects related to nutrition in an integrated way in the multidisciplinary treatment of Rett syndrome. The impact of approaches such as modifying food consistency, the use of thickeners, enteral feeding and vitamin and mineral supplementation are areas that require robust research to determine practices that really make a difference to patients' health and comfort. In addition, it is crucial to consider the psychological effect of these interventions on both patients and their families, who have to deal with the emotional repercussions and adjustments to routine that treatment entails (Vilvarajan et al., 2023).

Even so, eating and nutritional challenges are a significant part of the clinical management of Rett syndrome, due to the presence of dysphagia, oral motor difficulties, gastrointestinal problems and inadequate growth. Dysphagia, or difficulty swallowing, is common in patients with Rett syndrome, making it difficult to chew and swallow food, which increases the risk of aspiration and pneumonia, as well as contributing to malnutrition. Gastrointestinal problems, such as gastroesophageal reflux, constipation and abdominal distension, are also common and can interfere with the absorption of nutrients and comfort while eating. In addition, due to eating difficulties and the high energy demand associated with increased muscle tone, many patients experience growth problems, resulting in low weight and short stature (Motil et al., 2012).

To address these challenges, nutritional interventions include continuous assessment by nutritionists and specialized professionals to monitor the growth and nutritional status of patients. This assessment should include the use of specific growth charts and food intake analysis. It is clear that the oral route would be the best way of feeding, as it provides the necessary nutrition in a natural and pleasurable way, stimulates the senses of taste, smell and touch, and promotes social interaction during meals (Vilvarajan, et al., 2023).

However, due to the various motor and neurological difficulties that affect chewing and swallowing, specific strategies are needed to ensure safe and effective oral feeding. In some cases, for example, modifying the consistency of the food is relevant, preparing it in a paste-like consistency in order to facilitate swallowing and reduce the risk of choking. The use of thickeners for liquids, transforming them into safer consistencies, is also a common practice to prevent aspiration. However, despite the benefits, oral feeding presents challenges that must be managed carefully, such as swallowing dysfunction, which can lead to aspiration, causing serious respiratory problems. In addition, meals can be time-consuming and require patience from both the child and the caregivers. It follows that the oral route in Rett Syndrome requires

International Journal of Health Science ISSN 2764-0159 DOI https://doi.org/10.22533/at.ed.159522503012

a multidisciplinary and individualized approach, focused on modifying food consistency, safe feeding techniques and educating caregivers (Fu et al., 2020).

Vitamin and mineral supplements may also be necessary to ensure adequate nutrient intake, especially when oral feeding is limited. Furthermore, there are cases where oral feeding is not safe. With this in mind, the enteral route can be implemented. There are two main routes of enteral feeding: the nasogastric tube (NGT) and the percutaneous endoscopic gastrostomy (PEG). The nasogastric tube is a tube inserted through the nose into the stomach, generally used for short-term feeding, for example during an acute illness or recovery from surgery (Motil, et al., 2012).

Gastrostomy involves the insertion of a tube directly into the stomach through an opening in the abdominal wall, carried out by an endoscopic procedure . It is indicated for long-term feeding, when the need for nutritional support is continuous. It is often used in cases of malnutrition or risk of malnutrition, when oral feeding is not enough to maintain adequate growth and the child's nutritional status is compromised. In addition, it is used in situations of severe gastroesophageal reflux, when reflux causes significant problems and is not adequately controlled with dietary and drug interventions, as well as in severe gastrointestinal disorders, which make it difficult to absorb nutrients through oral feeding (Geerts, et al., 2019).

The implementation of enteral nutritional therapy begins with an initial multidisciplinary assessment, involving nutritionists, gastroenterologists and other health professionals to evaluate the child's clinical condition and determine the need for enteral feeding. Based on this assessment, an individualized nutritional plan is developed that meets the child's calorie, macronutrient and micronutrient needs. The selection and preparation of the enteral formula is another important step, where nutritional formulas developed for enteral feeding are used, which guarantee a balanced supply of nutrients and in some cases, homemade and personalized formulas can be prepared to meet specific nutritional needs or dietary restrictions. Ultimately, the enteral route offers significant benefits, such as ensuring that the child receives all the nutrients necessary for healthy growth and development, reducing the risk of aspiration associated with oral feeding in children with swallowing difficulties and improving general health status, growth and quality of life (Leonard et al., 2013).

It is clear that treatment is multidisciplinary and focused on symptom management, drugs such as anticonvulsants (valproate, levetiracetam, lamotrigine), baclofen and diazepam are used for spasticity, proton pump inhibitors for gastroesophageal reflux and melatonin for sleep disorders. These drugs can have significant interactions with nutrients and cause adverse effects that impact nutritional status, such as interference in the absorption of calcium and vitamin D by anticonvulsants, which can lead to osteoporosis, and reduced absorption of vitamin B12 and iron by omeprazole, resulting in nutritional deficiencies. It is therefore crucial that health professionals regularly monitor the nutritional status of patients with Rett syndrome (Fu, et al., 2020).

Although diet alone cannot reverse the neurological damage caused by Rett syndrome, proper, individualized nutrition can improve symptoms. Essential nutrients such as fatty acids, omega-3s, B vitamins and antioxidants play a key role in maintaining brain health. With a diet rich in these nutrients, it is possible to observe greater neurological stability, a reduction in the frequency and intensity of seizures, as well as a general improvement in cognitive and behavioral capacity. Therefore, nutritional management in Rett syndrome

must be essentially individualized and multidisciplinary, involving nutritionists, doctors, occupational therapists and speech therapists. Ongoing research and family education play a key role in implementing effective nutritional strategies (Geerts, et al., 2019).

Based on these considerations, this paper aims to conduct a comprehensive review of existing studies that address the role of diet and nutrition in the context of Rett syndrome. The research will seek to analyze nutritional disciplines with the potential to mitigate symptoms, contribute to growth and development and improve the general well-being of patients, offering a vision that can support the development of more appropriate guidelines and practices. In this way, we hope not only to broaden understanding of the nutritional management of Rett syndrome, but also to promote a more dignified quality of life for patients and provide practical and informed support for family members and caregivers.

METHODOLOGY

This is a narrative review of food and nutrition in Rett Syndrome, based on bibliographic research using the *National Library of Medicine* (Pubmed), *Scientific Electronic Library Online* (SCIELO), *Latin American and Caribbean Health Sciences Literature* (LILACS) and *Capes journals*.

A guiding question was defined as the basis for the research: "How can food and nutrition reduce and help with the symptoms of Rett Syndrome?". Based on this question, the following keywords were used in the research: "Rett Syndrome", "Rett Syndrome and nutrition", "Quality of life", "Adequate nutrition", "Epilepsy", "Gastrointestinal problems", "Nutritional therapy" and "Multidisciplinary treatment", using different combinations of these terms in order to promote greater scope and development of the research. The inclusion criteria for the selection of studies were defined as containing articles published between 2012 and 2024, which address nutrition and quality of life in patients with Rett Syndrome.

The exclusion criteria were studies that did not address food and nutrition issues. Opinion articles, editorials and letters to the editor were also excluded. Articles not in Portuguese, English or Spanish were also excluded. Finally, it was decided to discard studies published more than twelve years ago to ensure that the information reviewed was the most up-to-date and reflected the latest practices and knowledge.

RESULTS AND DISCUSSION

The bibliographic survey was carried out between March and June 2024, in the different databases described above, using the following descriptors: "Rett syndrome", "Rett syndrome and nutrition", "Quality of life", "Adequate nutrition", "Epilepsy", "Gastrointestinal problems", "Nutritional therapy" and "Multidisciplinary treatment". A combination of controlled descriptors was used to ensure a comprehensive and precise search. The initial search resulted in a wide range of potentially relevant studies.

In the first search, forty-eight (48) scientific articles were found by reading the titles and abstracts and analyzing the year of publication. Twenty-two (22) of these were excluded, as they dealt only with the concept of rett syndrome, which is hardly related to the diet and nutrition of this public. In this screening phase, a data collection method was developed, including the following variables: year of publication, article title, general objective, methodological basis, study model and conclusion. Of the twenty-six (26) articles, their full texts were read and twelve (12) were excluded because they did not meet the pre-established inclusion criteria. It should be noted that duplicate studies were discarded, resulting in fourteen (14) articles being selected.

In the final screening, the high number of exclusions can be attributed both to the careful analysis and to the scarcity of studies dealing with the subject in question. This rigorous selection is fundamental in scientific research aimed at composing a narrative review, as it aims to include only the most robust and relevant articles in the analysis. This ensures the validity of the results and enables a critical evaluation based on the technical quality and reliability of previously published studies.

Rett Syndrome (RS) is widely associated with mutations in the MECP2 gene (Methyl CpG Binding Protein 2), which is located on the X chromosome. This is a crucial gene for neuronal development and function, since it codes for a protein that binds to methylated DNA sequences and regulates the expression of other genes. Mutations in this gene can lead to a range of neurological dysfunctions, since the MECP2 protein plays a vital role in synaptic maturation and neuronal plasticity. In addition, the majority of MECP2 mutations in patients with RS are missense mutations, which result in the production of a protein that doesn't work properly or in the loss of the functional protein. It's worth noting that SR is more frequently observed in women due to its location on the x chromosome. Hemizygous males with a mutation are generally not viable, but there are several non-lethal mutations that can lead to severe congenital encephalopathy and intellectual disability in males (Lyst et al., 2015).

Problems with oral motor control and coordination are some of the first manifestations that make feeding difficult for patients with Rett Syndrome, which compromises the adequate intake of nutrients and increases the difficulty of swallowing. This makes feeding a challenging and often dangerous activity, due to the risk of aspiration and choking. This condition is amplified by the spasticity and muscle rigidity characteristic of the syndrome, which make it difficult to coordinate the movements essential for eating and digestion (Baikie et al., 2014).

In addition, the *MECP2* mutation also impacts the gastrointestinal system, causing conditions such as gastroesophageal reflux, which results from impaired neuromuscular function of the esophageal sphincter, increasing the risk of discomfort, regurgitation and, in some cases, malnutrition due to food refusal. And also constipation, which is a consequence of low intestinal motility and can be associated with both hypomobility and the use of medication, such as anticonvulsants. Thus, it is understood that these gastrointestinal challenges have a direct impact on the nutritional status and quality of life of patients, requiring continuous monitoring and early intervention strategies (Motil et al., 2012).

SR presents a series of nutritional challenges that directly affect the growth and development of patients, including a high prevalence of short stature and underweight. These problems often result from the high energy demand caused by motor complications such as spasticity, which increases basal energy expenditure, and other neuromotor disorders that make it difficult to eat properly. Patients with Rett syndrome also have difficulties in ingesting and absorbing nutrients, which increases the risk of malnutrition (Baikie et al., 2014).

In addition to calories and macronutrients, the need for micronutrients such as calcium and vitamin D deserves special attention, as patients with RS have a high risk of osteoporosis and fractures due to low bone density, which is common among girls with the syndrome. Low mobility and physical inactivity due to motor difficulties also contribute to a decrease in bone mass, which can be aggravated by a lack of adequate sun exposure and insufficient intake of these essential nutrients. Thus, the adequacy of these nutrients is essential for immune function and fighting in-

fections, considering that the immune system tends to be more vulnerable. Vitamin D, for example, plays an important role in strengthening the immune response and is a valuable support for the general health of these patients (Motil et al., 2012).

Due to the high prevalence of associated motor and neurological disorders, such as dystonia which causes involuntary, repetitive muscle contractions that can be painful, RS has significant impacts on basal metabolism which tends to be elevated in many cases, driven by muscle spasticity, rigidity and the involuntary movements characteristic of the syndrome. This increase in energy demand, even at rest, can aggravate the risk of malnutrition and weight loss, especially if nutritional needs are not adequately met (Motil et al., 2012)

And because of their high energy expenditure and limited food intake, patients with SR are at high risk of low body mass and loss of muscle mass over time. Maintaining a healthy body composition is essential, but challenging, due to the imbalance between calorie intake and energy consumption exacerbated by low muscle mass. This is because most of the girls are bedridden and many cannot afford therapies to maintain muscle tone (Kerr et al., 2016).

With feeding challenges, low nutrient absorption, the enteral route often becomes a key strategy, especially when there are swallowing difficulties, dysphagia and malnutrition, as it is an effective way of ensuring the nutritional support needed for growth and general health. Patients with Rett Syndrome often face oral motor coordination problems, dysphagia, and risk of aspiration, which can make safe and effective feeding a significant challenge. In cases where oral intake is not sufficient to meet nutritional needs, enteral feeding, via nasogastric tube or gastrostomy, offers a viable and safe alternative for providing essential nutrients (Motil et al., 2012).

The choice between enteral feeding routes, such as nasogastric tube and gastrostomy, depends on each case, such as the duration of feeding difficulties and each patient's condition. The nasogastric tube is generally indicated for short-term interventions, as it is a less invasive procedure, but it can cause long-term discomfort and impair food acceptance when used continuously. On the other hand, gastrostomy is preferred for long-term interventions, as it is a technique that allows for greater patient comfort, reducing the risk of infections and respiratory complications (Geerts et al., 2019).

The decision to start gastrostomy involves a careful analysis of various clinical factors, and is usually indicated in patients who have chronic malnutrition, significant weight loss or persistent difficulty in meeting nutritional needs through the oral route. Articles show that gastrostomy can significantly improve nutritional status. However, it is important that this intervention is accompanied by individualized nutritional planning, taking into account the specific needs of each patient so that enteral feeding can adequately meet energy and nutritional requirements. Despite the nutritional benefits, the implementation of enteral feeding, especially gastrostomy, can have a psychological impact on both the patient and the caregivers. Many caregivers report feelings of guilt for not being able to feed their child orally, which requires appropriate psychological support to help them accept this method (Leonard et al., 2013).

It is therefore extremely important to mention the role of the nutritionist in the transition from oral to enteral feeding, which is essential to ensure the adequacy and safety of this nutritional support. This professional carries out a thorough assessment of the patient's nutritional status, considering factors such as clinical condition, energy and protein needs, and the risks associated with the use of enteral nutrition, such as metabolic complica-

tions or intolerances gastrointestinal. In addition, the nutritionist is also responsible for selecting the most appropriate enteral formula, adjusting the calorie composition and volume based on the patient's individual specificities (Leonard et al., 2013).

In addition, the nutritionist plays a crucial role in preventing and managing common complications during the transition, such as refeeding syndrome, hydroelectrolyte disturbances and gastrointestinal changes, including nausea, diarrhea or constipation. Educating caregivers and family members is another relevant aspect, as they often take over the administration of enteral support in the home environment. In this sense, the nutritionist acts as an educator, providing guidance on administration techniques, care of feeding devices and identifying signs of intolerance. Thus, in a scenario where enteral nutrition is implemented early and in a planned manner, under the supervision of a nutritionist, the benefits include maintaining or recovering nutritional status, preventing complications and improving the patient's quality of life. Therefore, the presence of this professional throughout the transition process is essential for the success of nutritional therapy and for comprehensive patient support (Leonard et al., 2013).

The use of medication, especially anticonvulsants, plays an essential role in controlling epileptic seizures and other neurological complications. However, prolonged use of these drugs is often associated with side effects that can compromise nutritional status, such as reduced absorption of essential nutrients and interference in the synthesis of vitamins and minerals. Careful monitoring of these adverse effects is essential for adjusting the diet plan and avoiding nutritional deficiencies that could further aggravate the patients' clinical condition (Tarquinio et al., 2017).

Among the most commonly used anticonvulsants are valproic acid, phenytoin and carbamazepine, which are known to negatively impact bone density, a relevant concern for patients with Rett syndrome, who are already at increased risk of osteoporosis. These drugs can interfere with the absorption of calcium and vitamin D, as seen in another study, are critical nutrients for bone health, and can impair bone remodeling, leading to an increased risk of fractures and reduced bone mineral density over time. To mitigate these effects, frequent monitoring of the levels of these nutrients is recommended and, when necessary, targeted supplementation to ensure that daily needs are met (Motil et al., 2012).

In addition, these drugs can have a direct impact on metabolic health, compromising liver function and interfering with the synthesis of fat-soluble vitamins such as vitamins A, D, E and K. Patients taking anticonvulsants for a long time are at risk of deficiency of these vitamins, which play essential roles in the body, such as immunity, blood clotting and cell metabolism. Some patients may experience a loss of appetite, while others may face gastrointestinal difficulties, such as nausea and constipation, which make it difficult to eat properly. These adverse reactions directly influence the calorie and protein intake needed for growth and development, requiring a personalized nutritional approach that can help maintain energy balance. In some cases, the use of nutritional supplements and hypercaloric formulas is necessary to compensate for insufficient food intake and ensure that nutritional needs are met (Tarquinio et al., 2017; Motil et al., 2012).

In summary, it is important to mention that research on nutrition and diet in Rett Syndrome still has significant gaps that need to be addressed in order to provide better clinical practices and specific nutritional guidelines for patients. Currently, many available studies focus on describing the symptoms and clini-

cal manifestations of the syndrome, but there is a lack of data from controlled studies investigating effective nutritional interventions and their long-term impact on the health and quality of life of these patients. One of the limitations observed is the lack of standardized guidelines to help health professionals monitor the nutrition of girls with Rett syndrome, reflecting the need for investment in more detailed and specific studies.

The lack of clear guidelines for food and nutrition also indicates the need to explore different dietary approaches and strategies that meet the unique energy and metabolic demands of this population. The peculiarities of the syndrome, such as increased energy expenditure due to spasticity and gastrointestinal problems that hinder nutrient absorption, justify the search for personalized nutritional approaches. However, the small number of studies focusing on adapted dietary practices limits the development of specific recommendations. Thus, more research is needed to assess how different nutritional interventions, including micronutrient supplementation and the use of enteral feeding, impact the nutritional status and overall development of patients.

Finally, there is a growing need for studies investigating the role of multidisciplinary support and the interaction between nutrition, speech therapy, physiotherapy and occupational therapy professionals, among others, in the care of patients with Rett syndrome. Understanding the syndrome from a comprehensive perspective, including the interactions between nutritional and physical therapies, can help create more integrated treatment protocols that take into account nutrition as well as motor and gastrointestinal support. The implementation of epidemiological studies can provide data of greater validity and reliability, supporting the creation of public policies and specific clinical guidelines that facilitate the nutritional care of patients with Rett syndrome.

FINAL CONSIDERATIONS

This paper presented a literature review on the main aspects related to food and nutrition in Rett Syndrome, highlighting the essential role of nutritional intervention in improving the health and quality of life of these individuals. The analysis of characteristic dietary challenges, such as chewing and swallowing difficulties, altered energy needs and vulnerability to nutritional deficiencies, highlighted the complexity of nutritional care for people with Rett Syndrome.

As discussed, the risk of malnutrition and the deficiency of essential nutrients are common problems that directly affect the physical and neurological development of these patients. For this reason, personalized nutritional strategies, which take into account metabolic, digestive and motor particularities, are crucial to minimizing risks and ensuring adequate nutrient intake. In addition, micronutrient supplementation, when carried out individually and under specialized monitoring, can significantly contribute to improving clinical conditions, although it must be handled with caution to ensure the safety and efficacy of the treatment.

Furthermore, the importance of multidisciplinary action in the treatment of these patients is highlighted. In this context, education and support for caregivers is essential, since they are responsible for implementing the strategies defined by the multidisciplinary team. Offering regular training, clear guidelines and emotional support to caregivers is crucial to ensure that interventions are implemented effectively and safely in the home environment. The active involvement of caregivers also promotes more comprehensive and humanized management, in line with the individual needs of each patient.

Despite the progress made, there are still significant gaps in the literature regarding the long-term impact of nutritional interventions and the diet of patients with Rett Syndrome. Future studies could deepen knowledge about the specific needs of this population and contribute to the formulation of more precise, evidence-based guidelines.

Finally, it is hoped that this review will serve as a tool for health professionals and researchers, offering an understanding of the importance of nutrition and diet in Rett Syndrome and encouraging the development of practices that increasingly effectively meet the needs of this population. With continued research and the adoption of innovative approaches, it will be possible to promote a better quality of life for individuals with Rett Syndrome and their families.

REFERENCES

1 ARANCIBIA, T.; PARDO, R.; BARRIENTOS, P. **Síndrome de Rett, una mirada actual.** v. 94, n. 1, p. 94–94, 21 fev. 2023.

2 BAIKIE, G. et al. **Gastrointestinal Dysmotility in Rett Syndrome.** Journal of Pediatric Gastroenterology & Nutrition, v. 58, n. 2, p. 237–244, fev. 2014.

3 FU, C. et al. **Consensus guidelines on managing Rett syndrome across the lifespan.** BMJ Paediatrics Open, v. 4, n. 1, p. e000717, set. 2020.

4 GEERTS, S. **Nutrition Strategies for Rett Syndrome.** International Rett Syndrome Foundation, 2019. Disponível em: <https://www.rettsyndrome.org/for-families/education/nutrition/>. Acesso em: 14 jun. 2024.

5 KYLE, S. M.; VASHI, N.; JUSTICE, M. J. **Rett syndrome: a neurological disorder with metabolic components.** Open Biology, v. 8, n. 2, p. 170216, fev. 2018.

6 LEONARD, H. et al. **Improving health outcomes in Rett syndrome An information booklet for families and carers Nutritional and Digestive Health.** [s.l: s.n.], 2013.

7 LYST, M. J.; BIRD, A. **Rett syndrome: a complex disorder with simple roots.** Nature Reviews Genetics, v. 16, n. 5, p. 261–275, 3 mar. 2015.

8 MOTIL, K. J. et al. **Gastrointestinal and Nutritional Problems Occur Frequently Throughout Life in Girls and Women with Rett Syndrome.** Journal of pediatric gastroenterology and nutrition, v. 55, n. 3, p. 292–298, 1 set. 2012.

9 TARQUINIO, D. C. et al. **Longitudinal course of epilepsy in Rett syndrome and related disorders.** Brain, v. 140, n. 2, p. 306–318, 1 fev. 2017.

10 VILVARAJAN, S. et al. **Multidisciplinary Management of Rett Syndrome: Twenty Years' Experience.** Genes, v. 14, n. 8, p. 1607–1607, 11 ago. 2023