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Monogenic Obesity in Children: Current Perspectives and Clinical Implications

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ABSTRACT

Introduction: Monogenic obesity is characterized by a mutation in a single gene, which directly influences metabolism, appetite control or other biological pathways associated with body weight regulation**.**

Objective: To provide practical insights for healthcare professionals working with affected children to improve health outcomes and quality of life.

Methods: This study constitutes a systematic review, classified as exploratory and descriptive. The preparation of the research was a bibliographical search in electronic databases on methods associated with RSL (Systematic Literature Review) and the applications of SMARTER (*Simple Multi-Attribute Rating Technique using Exploiting Rankings*).

Results: A comprehensive systematic search of the literature yielded a total of 4125 articles referring to the incidence of obesity and overweight in adolescents, of which 20 articles were eligible to be included in this systematic review.

Conclusion: With a continued and coordinated effort, it is possible to significantly improve health outcomes for these children, preparing them for a brighter future.

KEYWORDS: Monogenic Obesity, Children, Genetics, Clinical Perspectives

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INTRODUCTION

Childhood obesity is a growing global epidemic with significant implications for public health and children's well-being. While many cases of obesity are multifactorial, a small proportion are attributed to a specific genetic condition known as monogenic obesity (KANSRA; LAKKUNARAJAH; JAY, 2021).

Monogenic obesity is characterized by a mutation in a single gene, which directly influences metabolism, appetite control or other biological pathways associated with body weight regulation (GASQUES et al., 2022). Although relatively rare, the identification of these mutations has profound implications for the diagnosis and management of obesity in children, providing crucial insights into the underlying mechanisms of this condition (LITTLETON; BERKOWITZ; GRANT, 2020).

Recent advances in genetic sequencing technology have provided a better understanding of the genetic basis of monogenic obesity, allowing a more precise and personalized approach to diagnosis and clinical management. However, significant challenges remain in interpreting genetic data, identifying pathogenic variants, and translating these findings into effective therapeutic interventions (LOOS; YEO, 2022; NASYKHOVA et al., 2019) . Genetic heterogeneity and the complexity of genetic and environmental interactions can make the diagnosis and clinical management of these cases difficult (FITCH; MALHOTRA; CONROY, 2024). As we continue to unravel the mechanisms underlying monogenic obesity, it is critical to integrate multidisciplinary and

collaborative approaches involving geneticists, endocrinologists, nutritionists, and other healthcare professionals to optimize care for these children (KUMARI et al., 2023).

This type of obesity in children is not just a physical health issue, but can also have a significant impact on psychosocial well-being. Affected children often face emotional challenges such as low self-esteem, social isolation and even discrimination due to their weight. These factors can contribute to mental health problems such as anxiety and depression, which in turn can perpetuate the cycle of obesity (HAQQ et al., 2021). Therefore, it is essential to take a comprehensive approach to treating monogenic obesity that not only addresses the physical issues but also takes into account the psychosocial and emotional impact on the child's overall health.

Furthermore, early diagnosis and adequate management of monogenic obesity in children may have long-term implications for adult health (MALHOTRA; SIVASUBRAMANIAN; SRIVASTAVA, 2021). Studies suggest that obesity in childhood is associated with a greater risk of developing chronic diseases such as type 2 diabetes, cardiovascular disease and certain types of cancer in adulthood (DROZDZ et al., 2021; KERAMAT et al., 2021). Therefore, effective interventions during childhood can not only help control weight and improve a child's immediate health, but can also have lasting benefits in reducing the risk of chronic diseases and promoting healthy aging.

An in-depth understanding of monogenic obesity is essential to offering personalized and effective care to affected children. This includes early identification through specific genetic testing and implementation of therapeutic strategies that target the underlying genetic changes. Furthermore, a comprehensive understanding of this condition may contribute to the development of new therapeutic approaches and more effective preventive interventions.

In this context, the aim of this article is to provide practical insights for healthcare professionals working with affected children, aiming to improve health outcomes and quality of life.

METHODS

This study constitutes a systematic review, classified as exploratory and descriptive. The preparation of the research was a bibliographical search in electronic databases on methods associated with RSL (Systematic Literature Review) and the applications of SMARTER (*Simple Multi-Attribute Rating Technique using Exploiting Rankings*). The work carried out is of a qualitative and quantitative nature. Qualitative data analysis was carried out intuitively and inductively during the survey of the theoretical framework. It is also quantitative through the use of the multi-criteria method. In addition, there is also a numerical experimental study in order to simulate an article selection situation based on the observed criteria.

The bibliographical research was carried out in the following databases: *Web of Science; Science Direct; Wiley; SpringerLink; Taylor and Francis; PubMed and EBSCO*. In addition, searches were carried out using bibliographical references of studies that relevantly addressed the topic on the *Google Scholar search platform*.

The search in the databases was carried out using the terminologies registered in the Health Sciences Descriptors created by the Virtual Health Library developed from the *Medical Subject Headings of the US National Library of Medicine*, which allows the use of common terminology in Portuguese, English and Spanish. The present study sought to investigate the literature on monogenic obesity in children and its clinical perspectives. To this end, the descriptors "Monogenic Obesity", "Children", "Genetics", "Clinical Perspectives" were used, initially in English, and in a complementary way in Spanish and Portuguese.

As a tool to support decision-making in the selection and prioritization of articles, a set of criteria were considered essential to represent the state of the art of the topic under study. This method has the following characteristics: (i) rigorous logic allows the method to be accepted as a decision support tool; (ii) simple to understand and apply with easy-to-interpret results.

References from selected works were also searched for other documents of potential interest. Once qualified for full text in the evaluation, articles were included in the qualitative review if they met the following inclusion criteria: a) contained data on monogenic obesity; b) contained data on obesity in children. Articles were excluded if they were reports, banners or conference abstracts. There was no review of confidential health information and the study was non-interventional. Therefore, ethics committee approval was not necessary. In the end, the result obtained totaled 20 articles that covered the desired characteristics for the study.

Three independent researchers extracted data from articles that met the inclusion criteria and recorded them in a "Data Extraction Form" generated in Microsoft Excel on monogenic obesity in children.

RESULTS

A comprehensive systematic search of the literature yielded a total of 4125 articles referring to the incidence of overweight and obesity in adolescents. Of these, 1153 studies were excluded due to data overlap. From this, the SMARTER method (*Simple Multi-Attribute Rating Technique using Exploiting Rankings)* was chosen and 434 articles were selected that were suitable for full-text screening, of which 196 articles were included for data extraction, of which 176 were excluded by the exclusion criteria, making 20 articles eligible and included for systematic review. In Figure 1, we describe the strategy for selecting articles on the topic in question.

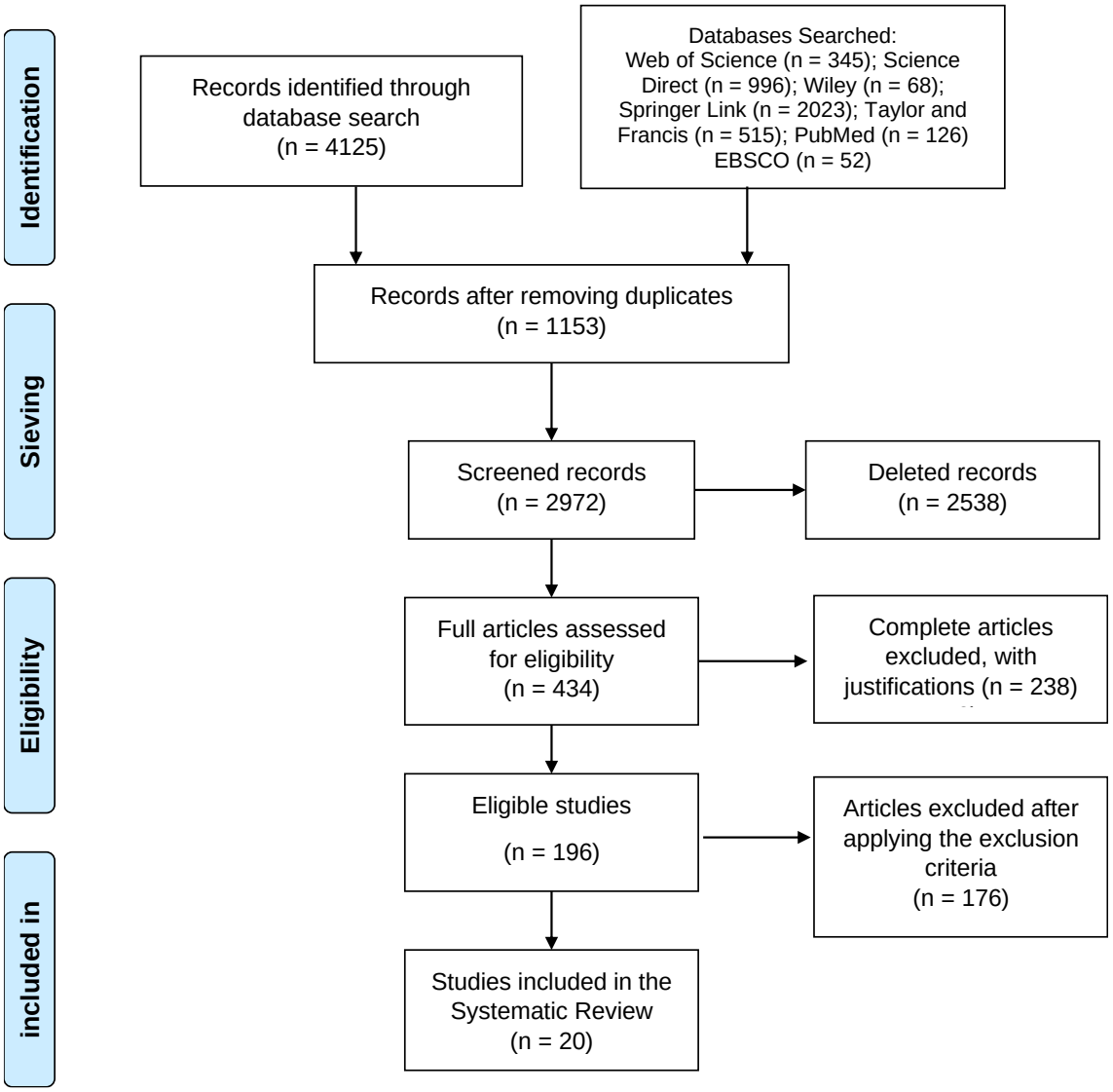

Figure 1. Article search strategy
Source: Authors (2024)

DISCUSSION

Recent studies have used next-generation sequencing (NGS) techniques to identify genetic variants associated with monogenic obesity in children. For example, a study published in 2022 used NGS to analyze genes related to energy metabolism and found new mutations in genes such as LEP, MC4R, LEPR, and POMC expanding knowledge about the genetic basis of this condition (NALBANTOĞLU et al., 2022). These discoveries are fundamental to understanding the underlying molecular mechanisms that regulate appetite and energy storage (SIVASUBRAMANIAN; MALHOTRA, 2023).

The complexity of the genetic mechanisms involved in monogenic obesity is another central point in the current discussion. Research indicates that the phenotypic expression of genetic mutations can be modulated by environmental and lifestyle factors. Some studies have discussed how gene-environment interaction influences the manifestation of obesity, suggesting that environmental interventions can modify the expression of genetic traits related to obesity (MAHMOUD, 2022). This emphasizes the need to consider environmental factors when developing management and prevention strategies.

In the clinical context, early diagnosis of monogenic obesity in children is crucial. A recent study highlighted the importance of genetic diagnosis to identify at-risk children and implement personalized interventions from an early age (SOHN, 2022) . However, genetic diagnosis also raises ethical and psychosocial questions. The first IMPROVE 2022 International Meeting addressed the challenges associated with genetic diagnosis, including stigma and the impact on children's self-esteem, suggesting that psychosocial support should be an integral part of clinical management (KÜHNEN et al., 2024).

Targeted therapies are advancing rapidly. Recent clinical studies have investigated the effectiveness of pharmacological treatments that target specific metabolic pathways affected by genetic mutations. Studies have demonstrated promising results with the use of MC4R agonists to treat obesity caused by mutations in this gene,

showing significant reductions in body mass index (BMI) and improvements in metabolic markers. (FANSA; ACOSTA, 2024). These treatments are still in the testing phase, but represent a significant advance in personalized therapy for monogenic obesity.

Early interventions are essential to prevent the full manifestation of obesity in genetically predisposed children. It is essential to emphasize the relevance of nutrition and physical activity programs, adapted to individual needs, as effective forms of early intervention (DROZDOVSKA et al., 2022). Furthermore, educating parents and communities about healthy habits is essential to the success of these preventive strategies.

Developing public health policies that support healthy environments for children is essential. Addressing the relevance of stricter regulations on the marketing of unhealthy foods and improvements in access to nutritious foods in schools and communities is essential (SING et al., 2023). Furthermore, educational policies that promote healthy habits from an early age are vital to combat childhood obesity effectively (DIETZ; BAUR, 2022).

The approach to treating monogenic obesity in children must integrate advances in genetic research, personalized clinical interventions, and comprehensive public health policies, requiring collaboration among researchers, healthcare professionals, educators, policymakers, and communities. The goal is to reduce the prevalence and negative impacts of this condition, improving children's health and quality of life and preparing them for a healthier future, through continuous research, therapeutic innovation and prevention strategies.

FINAL CONSIDERATIONS

Monogenic obesity in children highlights the need for a multidisciplinary and collaborative approach to tackling this complex condition. Integrating advances in genetic research with personalized clinical interventions and comprehensive public health policies is critical to delivering effective treatment. Early identification and accurate diagnosis, together with targeted therapies, are essential to manage this pathology efficiently and improve the quality of life of affected children.

It is crucial that researchers, healthcare professionals, educators, policymakers, and communities work together to create a stable, supportive environment. This collaboration not only facilitates the development and implementation of clinical interventions, but also promotes education and awareness about monogenic obesity. Preventative and therapeutic programs tailored to individual genetic needs can reduce negative impacts and help control the prevalence of this condition.

Continued research plays a central role in understanding and treating monogenic obesity. Recent advances in genetic sequencing technologies have allowed the identification of new mutations associated with this condition, expanding the possibilities for specific therapeutic interventions. Furthermore, therapeutic innovation, including new medications and dietary approaches, shows promise in managing the disease.

Implementing public health policies that promote healthy environments for children is equally important. This includes regulating the marketing of unhealthy foods, improving access to nutritious foods, and promoting healthy lifestyle habits from an early age. Educational policies that encourage regular physical activity and a balanced diet are essential to effectively combat childhood obesity.

The objective is to reduce the prevalence and negative impacts of monogenic obesity in children, providing them with a healthier and better-quality life. Continuity in research, therapeutic innovation and the application of prevention strategies play crucial roles in achieving this goal. With a continued, coordinated effort, it is possible to significantly improve health outcomes for these children, preparing them for a brighter future.

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