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NEXT GENERATION SEQUENCING IN NEONATAL SCREENING: ADVANCES AND CHALLENGES IN THE EARLY IDENTIFICATION OF GENETIC DISORDERS

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Abstract: Next-generation sequencing (NGS) represents a milestone in neonatal screening, allowing for greater diagnostic accuracy and broadening the spectrum of detectable genetic conditions . This study reviewed the advantages of NGS compared to traditional methods, highlighting its impact on the early detection of genetic and metabolic disorders, with the potential for earlier and more personalized clinical interventions. Twenty-five articles published between 2020 and 2024 on the PubMed database were selected. The results highlight that NGS reduces limitations such as false positives and late diagnosis, improving neonatal outcomes. However, challenges remain, including high costs, lack of infrastructure in low-income regions and ethical issues related to confidentiality and accessibility. The standardization of genetic panels and the training of professionals are essential to enable their widespread adoption. It is concluded that NGS offers an innovative approach to neonatal screening, with the potential to transform clinical practice and public health programs. Public policies and global collaborations are needed to democratize access and maximize the benefits of this technology.
Keywords: next-generation sequencing, neonatal screening, genetics, public health.

INTRODUCTION

The use of advanced technologies for neonatal screening has been consolidated as an essential area of public health, allowing the early identification of genetic and metabolic disorders (Huang *et al*., 2022). Since the introduction of the tandem mass spectrometer (MS/MS) in the 1980s, significant advances have been made, making it possible to broaden the scope of conditions detected through a single biochemical test (Wang *et al*., 2021). Next-generation sequencing (NGS), in turn, represents a promising development, providing greater diagnostic accuracy and expan-

ding the screening capacity for conditions previously undetectable by traditional methods (Huang *et al*., 2022). This scenario highlights the importance of exploring integrated technological solutions to optimize neonatal screening programs.

Currently, conventional neonatal screening methods face significant limitations, such as high false positive rates and late diagnoses, which can delay crucial clinical interventions. For Veldman *et al*. (2022), the use of NGS in conjunction with traditional biochemical approaches allows these limitations to be overcome, offering faster and more reliable results. Despite this, major challenges remain, including ethical issues and high costs associated with large-scale implementation.

Although next-generation sequencing represents a technological leap forward, important gaps still need to be addressed. According to Bick *et al*. (2019), there is an urgent need for more comprehensive panels that include relevant clinical variants, as well as solutions that make the technology economically viable for public health programs. This gap is particularly relevant in regions where resources for neonatal screening are limited, reinforcing the need to optimize and adapt NGS panels for different populations.

Recent advances demonstrate the potential of genomic sequencing to transform neonatal screening. According to Mujamammi *et al*. (2022), studies with NGS panels show superior accuracy in detecting inborn errors of metabolism, reducing diagnosis time and enabling earlier interventions. For Yang *et al*. (2023), the implementation of NGS can also contribute to a broader and more effective approach to identifying complex genetic conditions, promoting greater personalization of neonatal care. In addition, the ability to detect diseases even before symptoms appear could radically change the neonatal health landscape.

For Veldman *et al*. (2022), comparative studies between NGS and conventional methods indicate a clear superiority of next-generation sequencing, especially in the identification of rare conditions. However, issues such as data confidentiality and affordability remain major barriers to its widespread adoption. Wang *et al*. (2021) reinforce that initiatives such as the NeoSeq project demonstrate the potential of simplified technologies for genomic screening, combining cost-effectiveness with high diagnostic accuracy.

The aim of this study is to evaluate the effectiveness of next-generation sequencing in neonatal screening for genetic disorders, comparing the results with traditional methods. The research also seeks to explore the clinical, ethical and economic implications of incorporating this technology into public health programs, contributing to the improvement of neonatal screening globally.

METHODOLOGY

This is a literature review developed according to the criteria of the PVO strategy, which stands for: population or research problem, variables and outcome. This strategy was used to develop the research question "Does the use of next-generation sequencing (NGS) panels improve the accuracy of neonatal screening for genetic disorders compared to conventional methods?". The searches were carried out using the PubMed - MEDLINE (Medical Literature Analysis and Retrieval System Online) databases. The search terms were used in combination with the Boolean terms "AND" or "OR", using the following search strategy: (neonatal inborn disorders) AND ((next generation sequencing) OR (NGS)). From this search, 89 articles were found, which were then submitted to the selection criteria. The inclusion criteria were: articles published between 2020 and 2024 that addressed the themes proposed for this research, observational studies and experimental studies. The exclu-

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sion criteria were: duplicate articles, articles available in abstract form, articles that did not directly address the proposal studied and articles that did not meet the other inclusion criteria. After applying the search strategy to the database, a total of 31 articles were found. After applying the inclusion and exclusion criteria, 25 articles were selected from the PubMed database to make up this study's collection.

DISCUSSION

Advances in the application of next-generation sequencing (NGS) in neonatal screening have revealed important contributions to the early detection of genetic disorders. According to Zhang *et al*. (2023), NGS has demonstrated superior ability to identify genetic variants associated with rare diseases, allowing for more accurate and rapid diagnoses. This method is widely recognized as an essential tool for reducing the limitations of traditional methods, such as false positives and late diagnoses (Kim *et al*., 2023). This technology, in addition to promoting advances in the field of genetic medicine, has had a significant impact on clinical practice, especially in rare and complex conditions that defy conventional systems. The impact of this advance is reflected in greater diagnostic accuracy, as well as making it possible to detect genetic anomalies at earlier stages, thus expanding the possibilities for early clinical intervention.

For Ibarra-González *et al*. (2020), NGS offers a powerful solution for detecting genetic conditions at early stages, which can significantly reduce morbidity rates in neonates. This corroborates the advances reported in other studies that highlight the relevance of the clinical application of NGS. This approach also favours the personalization of care, allowing targeted interventions based on individual genetic profiles. Furthermore, the use of NGS is not limited to diagnosis, but also helps to map genetic inheritance, contributing to long-term public health programs.

However, studies such as those by Soriano-Sexto *et al*. (2022) highlight challenges in implementing NGS on a global scale, including high costs and ethical barriers related to unequal access to the technology. These challenges are particularly evident in low- and middle-income regions, where resources for neonatal screening programs are limited (Elsink *et al*., 2022). Inequality in access is a critical point that reflects global disparities and requires innovative solutions and international collaboration to overcome. This highlights the need for integrated policies that seek not only to expand access, but also to democratize technology-based healthcare.

The comparison between traditional methods and NGS is a central point in the literature reviewed. For Wang *et al*. (2020), while traditional methods continue to be widely used due to their low cost and accessibility, they have significant limitations in terms of diagnostic accuracy. On the other hand, Nardecchia *et al*. (2022) point out that NGS not only broadens the spectrum of detectable diseases, but also improves the accuracy and reliability of diagnoses. The technical superiority of NGS becomes evident especially in conditions where early identification can significantly alter clinical outcomes. This accuracy is key to mitigating the impacts of late treatment and reducing the burden on healthcare systems.

According to Kose *et al*. (2021), NGS is significantly more accurate than traditional methods, making it possible to detect rare conditions more effectively. This superiority is evidenced in studies that highlight its ability to reduce false negatives in diagnoses of inborn errors of metabolism. In addition, NGS offers the opportunity to create more robust genetic databases, which can enrich future research. The availability of more extensive genetic data is also an essential foundation for advances in personalized medicine, allowing for more effective and targeted approaches.

Studies such as those by Barbosa-Gouveia *et al.* (2021) indicate a positive correlation between the use of NGS and a reduction in late diagnoses, especially in cases of metabolic disorders. However, it is important to recognize that this approach is not without its limitations, including the need to standardize genetic panels and the interpretation of results (Mao *et al.*, 2020). These technical and operational challenges are compounded by a lack of infrastructure and a shortage of trained professionals in many regions. It is therefore necessary to invest in training and continuous training for medical and technical teams.

The implications of the findings of this review are wide-ranging and include theoretical and practical contributions. For Migliavacca *et al.* (2024), the use of NGS contributes significantly to the advancement of knowledge in medical genetics, broadening the theoretical basis for future studies. In addition, the application of NGS has the potential to transform clinical practice, influencing public health guidelines and policies related to neonatal screening (Isler *et al.*, 2020). This transformation involves not only clinical improvements, but also a redefinition of the role of genetics in preventive medicine. This could catalyze change on a global scale, promoting more equitable and technologically advanced health.

On a practical level, the results suggest that incorporating NGS into health programs can significantly improve clinical outcomes, especially in high-risk populations. However, there is an urgent need to develop strategies to overcome the financial and ethical challenges associated with large-scale adoption (Sudrié-Arnaud *et al.*, 2021). For Engelbrecht *et al.* (2021), the introduction of NGS in neonatal screening programs not only improves diagnostic accuracy, but also offers an opportunity to implement earlier and more personalized treatments. This approach highlights the potential impact of technology in redefining neonatal health guidelines.

Based on the gaps identified, future research should explore the standardization of genetic panels and the economic viability of NGS in different contexts. Longitudinal studies evaluating the impact of NGS on neonatal health outcomes are also highly recommended (Tang *et al.*, 2024). These investigations can contribute to improving understanding of the clinical applications and effectiveness of NGS in diverse populations. In addition, interdisciplinary studies combining technical and ethical aspects could offer new perspectives and innovative solutions to current challenges.

According to Casertano *et al.* (2021), it is essential that future studies explore the combination of NGS with more robust ethical approaches, especially in contexts of vulnerable populations. Such research should seek solutions that balance the cost-effectiveness of the technology with its accessibility. For Śmigiel *et al.* (2020), it is essential to investigate approaches that integrate NGS with other diagnostic methods, creating more robust and accessible protocols. In addition, future research should consider the ethical and social impact of using genetic technologies in different cultural and economic contexts (Sheck *et al.*, 2021). These issues highlight the need for a broader global dialog about the limits and possibilities of applied genetics.

FINAL CONSIDERATIONS

Next-generation sequencing (NGS) presents a transformative advance in neonatal screening, offering greater diagnostic accuracy and broadening the spectrum of detectable genetic conditions. This study reviewed the advantages of NGS over traditional methods, highlighting its impact on the early identification of genetic and metabolic disorders, with the potential to significantly improve neonatal clinical outcomes. The application of NGS also promotes earlier and more personalized interventions, marking an important step in the integration of genetics into preventive medicine.

However, challenges remain, including the high cost of implementation, the lack of infrastructure in low-income regions and ethical issues related to the confidentiality of genetic data and accessibility. The need to standardize genetic panels and train trained professionals also stands out as a critical obstacle to their large-scale adoption.

The results of this review point to the importance of public policies that prioritize democratizing access to advanced technologies such as NGS, integrating them into neonatal screening programs in a cost-effective manner. In addition, future studies should focus on economic viability, long-term impacts on public health and the creation of robust ethical protocols to protect vulnerable populations.

Finally, the integration of NGS into neonatal screening not only improves diagnostic accuracy and comprehensiveness, but also reinforces the role of genetics in transforming neonatal care. With continued investment in research, infrastructure and global collaborations, NGS has the potential to set a new standard for neonatal screening, contributing to more equitable and technologically advanced neonatal health.

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