



Impacto da expressão de microrna no líquido amniótico como biomarcador precoce para distúrbios hipertensivos da gravidez

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ABSTRACT

Hypertensive diseases of pregnancy (HDP), such as pre-eclampsia and gestational hypertension, represent one of the main causes of maternal and fetal morbidity and mortality. Early identification of these conditions is essential for implementing therapeutic and monitoring strategies that can reduce serious complications. In this context, microRNAs (miRNAs), small molecules that regulate gene expression, have been widely studied as potential biomarkers. Analyzing the expression of miRNAs in amniotic fluid has emerged as a promising approach for the early detection of HGD, allowing for more effective and less invasive screening compared to traditional methods. The aim in question is to investigate the impact of miRNA expression in amniotic fluid as early biomarkers for hypertensive disorders of pregnancy, evaluating their association with pathophysiological changes and their clinical applicability in predicting these conditions. This study is a literature review with a qualitative approach, focused on investigating the role of microRNAs and hypertensive disorders in pregnancy. The research aims to understand how microRNAs can be used as diagnostic and therapeutic biomarkers in gestational complications, especially in pre-eclampsia and other hypertensive disorders of pregnancy. Recent studies have shown that the differential expression of miRNAs in amniotic fluid may be directly related to placental dysfunction and the development of GDM. Some miRNAs, such as miR-210, miR-155 and miR-517, have been associated with placental hypoxia and the activation of inflammatory pathways involved in the pathogenesis of pre-eclampsia. The ability of these miRNAs to modulate angiogenesis and endothelial function suggests their potential as predictive biomarkers. In addition, advanced sequencing techniques have enabled a more detailed analysis of the miRNA profile in amniotic fluid, facilitating the identification of specific patterns for each HGD phenotype. However, challenges such as the standardization of detection methods and clinical validation still need to be overcome before these tools can be implemented in obstetric practice. The expression of miRNAs in amniotic fluid has great potential as an early biomarker for hypertensive disorders of pregnancy, enabling a more accurate diagnosis and a more effective preventive approach. Despite the promising advances, more research is needed to validate these findings and establish clinical protocols that make their routine application feasible. Integrating these findings with other diagnostic approaches could represent a significant advance in the management of HGD, contributing to a reduction in maternal-fetal complications and improving obstetric outcomes.

Keywords: Hypertensive diseases in pregnancy, biomarkers, microRNA expression.

RESUMO

Doenças hipertensivas da gravidez (DHG), como pré-eclâmpsia e hipertensão gestacional, representam uma das principais causas de morbidade e mortalidade materna e fetal. A identificação precoce dessas condições é essencial para a implementação de estratégias terapêuticas e de monitoramento que possam reduzir complicações graves. Nesse contexto, microRNAs (miRNAs), pequenas moléculas que regulam a expressão gênica, têm sido amplamente estudadas como potenciais biomarcadores. Analisar a expressão de miRNAs no líquido amniótico tem se mostrado uma abordagem promissora para a detecção precoce de DGH, permitindo um rastreamento mais eficaz e menos invasivo em comparação aos métodos tradicionais. O objetivo em questão é investigar o impacto da expressão de miRNAs no líquido amniótico como biomarcadores precoces para distúrbios hipertensivos da gravidez, avaliando sua associação com alterações fisiopatológicas e sua aplicabilidade clínica na predição dessas condições. Este estudo é uma revisão de literatura com abordagem qualitativa, focada em investigar o papel dos microRNAs e dos distúrbios hipertensivos na gravidez. A pesquisa visa compreender como microRNAs podem ser utilizados como biomarcadores diagnósticos e terapêuticos em complicações gestacionais, especialmente na pré-eclâmpsia e outros distúrbios hipertensivos da gravidez. Estudos recentes têm demonstrado que a expressão diferencial de microRNAs no líquido amniótico pode estar diretamente relacionada à disfunção placentária e ao desenvolvimento de DMG. Alguns miRNAs, como miR-210, miR-155 e miR-517, têm sido associados à hipóxia placentária e à ativação de vias inflamatórias envolvidas na patogênese da pré-eclâmpsia. A capacidade desses miRNAs de modular a angiogênese e a função endotelial sugere seu potencial como biomarcadores preditivos. Além disso, técnicas avançadas de sequenciamento têm permitido uma análise mais detalhada do perfil de miRNAs no líquido amniótico, facilitando a identificação de padrões específicos para cada fenótipo de DGH. No entanto, desafios como a padronização de métodos de detecção e a validação clínica ainda precisam ser superados antes que essas ferramentas possam ser implementadas na prática obstétrica. A expressão de miRNAs no líquido amniótico tem grande potencial como biomarcador precoce para distúrbios hipertensivos gestacionais, permitindo um diagnóstico mais preciso e uma abordagem preventiva mais eficaz. Apesar dos avanços promissores, mais pesquisas são necessárias para validar esses achados e estabelecer protocolos clínicos que viabilizem sua aplicação rotineira. A integração desses achados com outras abordagens diagnósticas pode representar um avanço significativo no manejo da DGH, contribuindo para a redução das complicações materno-fetais e melhorando os desfechos obstétricos.

Palavras-chave: Doenças hipertensivas na gestação, biomarcadores, expressão de microRNAs.

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INTRODUCTION

Hypertensive disorders of pregnancy (HDP), such as pre-eclampsia and gestational hypertension, are serious conditions that affect approximately 10% of pregnant women worldwide, and are one of the main causes of maternal and fetal morbidity and mortality. Early identification of these conditions is essential to improve maternal and neonatal outcomes, reducing serious complications such as intrauterine growth restriction, prematurity and placental insufficiency (KHAN et al., 2021).

In recent years, the investigation of molecular biomarkers, such as microRNAs (miRNAs), has gained prominence in obstetrics, as these small regulatory molecules play a crucial role in modulating gene expression and placental physiology. Recent studies have shown that miRNAs present in amniotic fluid can reflect early pathological changes associated with the development of HGD, making them potential biomarkers for screening and early diagnosis of these conditions (TONG et al., 2023).

Analysis of the expression of miRNAs in amniotic fluid may allow the detection of alterations in the fetal environment before the clinical symptoms of gestational hypertension and pre-eclampsia appear (ZHANG et al., 2023). In this way, the identification of specific miRNA profiles can contribute to the development of minimally invasive diagnostic tests, as well as offering insights into the pathophysiological mechanisms involved in these diseases (CHENG et al., 2022).

Therefore, understanding the impact of miRNA expression in amniotic fluid as an early biomarker for hypertensive diseases of pregnancy represents a significant advance in maternal-fetal medicine. Based on this approach, new therapeutic and preventive strategies can be outlined, aiding in the early and personalized management of high-risk pregnant women (KARLSSON et al., 2021).

The aim of this study is to investigate the impact of the expression of miRNAs in amniotic fluid as early biomarkers for hypertensive disorders of pregnancy, assessing their association with pathophysiological changes and their clinical applicability in predicting these conditions.

MATERIALS AND METHODS

This study is a literature review with a qualitative approach, focused on investigating the role of microRNAs and hypertensive disorders in pregnancy. The research aims to understand how microRNAs can be used as diagnostic and therapeutic biomarkers in gestational complications, especially in pre-eclampsia and other hypertensive disorders of pregnancy.

- Guiding question:

What is the role of microRNAs as biomarkers in the detection and management of hypertensive disorders of pregnancy, including pre-eclampsia?

- Inclusion criteria:

- Publications between 2021 and 2023, ensuring that the findings are current.

- Studies on microRNAs, hypertensive disorders of pregnancy, diagnostic and therapeutic biomarkers.

- Papers available in full and indexed in PubMed, Scopus, Web of Science and SciELO.

- Studies in English, Portuguese or Spanish.

- Systematic reviews, experimental studies, clinical analyses and meta-analyses.

- Exclusion criteria:

- Studies published before 2021.

- Studies unavailable in full or not relevant to the topic.

- Studies focused exclusively on genetic factors unrelated to microRNAs.

- Articles on biomarkers other than microRNAs.

- Boolean markers:

- (“microRNA” AND “preeclampsia” AND “biomarker”).

- (“hypertensive disorders of pregnancy” OR “gestational hypertension”) AND (“microRNA”).

- (“placental dysfunction” AND “microRNA-based diagnosis”).

Theoretical background

Hypertensive disorders of pregnancy (HDP) represent one of the main challenges of modern obstetrics due to their high maternal and fetal morbidity and mortality. Among these conditions, pre-eclampsia and eclampsia stand out as the most serious forms, and can lead to severe

complications such as fetal growth restriction, premature birth, placental insufficiency and even maternal and neonatal death (Amaral et al., 2022).

Pre-eclampsia, in particular, is characterized by systemic endothelial dysfunction, leading to inflammation, increased vascular permeability and placental dysfunction, which can compromise fetal development. Early identification of these conditions is essential to optimize clinical management, reducing risks and enabling preventive interventions before the progression of gestational hypertension (Brown et al., 2023).

In recent years, microRNAs (miRNAs) have emerged as promising biomarkers for the early detection of various pathological conditions, including hypertensive diseases of pregnancy. miRNAs are small non-coding RNA sequences that play essential roles in regulating post-transcriptional gene expression, controlling fundamental cellular processes such as proliferation, apoptosis and inflammation. In the context of GDM, several studies have shown that the abnormal expression of certain miRNAs may be directly associated with the pathophysiology of pre-eclampsia, indicating their relevance both in diagnosis and in understanding the mechanisms underlying the disease (He et al., 2023).

Amniotic fluid is a rich biological source for identifying biomarkers, as it contains miRNAs derived from the fetus and placenta, dynamically reflecting the state of gestational health. Analysis of the profile of miRNAs in this biological fluid revealed altered patterns in pregnant women with

pre-eclampsia, suggesting that these molecules could serve as non-invasive diagnostic tools to identify women at risk of developing GDM. Among the most investigated miRNAs is miR-210, which is strongly associated with placental hypoxia, a central feature of pre-eclampsia. This miRNA plays a critical role in cellular adaptation to low oxygen levels, influencing angiogenesis and placental homeostasis. Its overexpression has been correlated with the vascular dysfunction observed in pre-eclampsia, reinforcing its potential as a biomarker for the disease (Chen et al., 2022).

Another miRNA of interest is miR-155, which has been associated with exacerbated inflammatory responses in pregnant women with pre-eclampsia. Studies indicate that the increased expression of this miRNA may be related to the activation of inflammatory and immunological pathways that contribute to the endothelial dysfunction characteristic of the disease. In addition, miR-517a-3p, which plays a role in placental development, also shows altered expression in women with GDM, reinforcing the importance of studying these biomarkers in elucidating the pathophysiological mechanisms of the disease (Moran-Pérez et al., 2023).

The identification of specific miRNA profiles in amniotic fluid could represent a significant advance in maternal-fetal medicine. The possibility of using these molecules as biomarkers for early screening of HGD offers a promising alternative to traditional diagnostic methods, which often rely on late clinical signs

such as hypertension and proteinuria. Recent studies indicate that the combination of multiple miRNAs can increase diagnostic accuracy and allow risk stratification in pregnant women, enabling more personalized and targeted management for each patient (Davis et al., 2022).

In addition to their diagnostic value, miRNAs are also being explored as potential therapeutic targets. Strategies aimed at modulating the expression of miRNAs involved in the pathophysiology of pre-eclampsia are being investigated as innovative approaches to mitigating the adverse effects of the disease. Therapy based on miRNAs could, for example, restore placental function by modulating signaling pathways critical for angiogenesis and the inflammatory response, thus improving maternal-fetal prognosis (Lee et al., 2021).

The growing understanding of the role of miRNAs in gestational biology reinforces the need for further studies to validate their clinical use as biomarkers and therapeutic targets. Clinical trials are essential to establish the reliability and reproducibility of miRNA signatures in amniotic fluid, ensuring that these biomarkers can be effectively incorporated into obstetric medical practice. The integration of miRNA analysis with other approaches, such as artificial intelligence and predictive models based on machine learning, can also enhance the early detection capacity of HGD and improve clinical decision-making (Moran-Pérez et al., 2023).

Thus, the study of miRNA expression in amniotic fluid represents an emerging field with the potential to transform the approach to hypertensive diseases of pregnancy. The identification of specific miRNA signatures could contribute to the development of earlier and more accurate diagnostic tests, as well as enabling new therapeutic interventions to reduce the impact of these diseases on maternal and fetal health. As research progresses, it is hoped that the incorporation of these biomarkers into clinical practice will lead to a significant improvement in the prognosis of pregnant women and a reduction in the complications associated with HGD (Torres et al., 2023).

CONCLUSION

We conclude that the impact of microRNA expression in amniotic fluid as an early biomarker for hypertensive diseases of pregnancy represents a significant advance in maternal-fetal medicine. The possibility of detecting molecular alterations before clinical symptoms appear opens up new perspectives for the early diagnosis and management of these conditions, allowing for more effective and targeted interventions to reduce maternal-fetal risks.

Studies on the regulation of microRNAs demonstrate their fundamental role in the pathophysiology of gestational hypertensive diseases, especially in pre-eclampsia. The identification of specific patterns of expression

of these biomarkers in amniotic fluid enables a less invasive and more accurate diagnostic approach, reducing dependence on conventional methods, which often detect the disease in late stages. Furthermore, incorporating these findings into clinical practice could significantly improve risk stratification and personalized care planning for vulnerable pregnant women.

In addition to their diagnostic potential, microRNAs are also emerging as possible therapeutic targets, broadening the prospects for the treatment of hypertensive diseases of pregnancy. The modulation of these biomarkers could help restore placental function and reduce the vascular damage associated with the condition, offering an innovative approach to minimize complications for both mother and baby.

Given these advances, it is essential that more research is conducted to validate the use of microRNAs as clinical and therapeutic biomarkers, ensuring their applicability in obstetric practice. Integrating this technology with other strategies, such as artificial intelligence and predictive models, could further improve early detection and personalized intervention. In this way, the incorporation of microRNAs into the clinical scenario could transform the management of hypertensive diseases of pregnancy, promoting a positive impact on maternal-fetal health and reducing the complication and mortality rates associated with these conditions.

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Observação: os/(as) autores/(as) declaram não existir conflitos de interesses de qualquer natureza.