Commentary
Volume 16:01, 2025

Human Genetics & Embryology

ISSN: 2161-0436 Open Access

Bidirectional Mendelian Randomization Analysis of Plasma Fatty Acids and their Role in Pre-eclampsia Risk

Genine Huang *

Department of Clinical Laboratory, Obstetrics and Gynecology Hospital of Fudan University, Shanghai 200090, China

Introduction

Pre-eclampsia (PE) is a significant pregnancy complication characterized by hypertension and proteinuria, affecting around 2-8% of pregnancies worldwide. It is a major cause of maternal and fetal morbidity and mortality. The exact pathophysiology of pre-eclampsia remains incompletely understood, but it is widely accepted that both genetic and environmental factors play key roles in its development. Among the environmental factors, diet and nutritional status, including the intake of fatty acids, have been suggested to influence the risk of developing pre-eclampsia. However, the exact nature of this relationship is unclear, particularly whether certain types of fatty acids have a causal role in the development of the disease. The field of genetic epidemiology has introduced a novel approach known as Mendelian Randomization (MR), which uses genetic variants as proxies (or instruments) for an exposure to assess the causal effect of that exposure on an outcome. This method is particularly useful in addressing confounding and reverse causality, common limitations in traditional observational studies. By utilizing genetic proxies for plasma fatty acids, MR can provide insights into whether fatty acids causally influence the risk of pre-eclampsia or vice versa. Bidirectional Mendelian randomization (BMR), which allows for the exploration of causal relationships in both directions, has the potential to shed light on how fatty acids and pre-eclampsia interact. This review explores the role of bidirectional Mendelian randomization in understanding the relationship between plasma fatty acids and pre-eclampsia, considering both the potential impact of fatty acids on PE risk and the possibility that PE may influence fatty acid metabolism.

Description

Fatty acids are essential components of the diet, influencing various physiological processes including membrane structure, inflammation, and cellular signaling. In the context of pregnancy, fatty acids are crucial for fetal development, particularly for the growth and development of the fetal brain and nervous system. The balance between omega-3 and omega-6 fatty acids is thought to be particularly important, with omega-3 fatty acids, such as Eicosapentaenoic Acid (EPA) and docosahexaenoic acid (DHA), being generally considered protective due to their anti-inflammatory properties. Omega-6 fatty acids, on the other hand, may promote inflammation, which has been associated with the pathogenesis of pre-eclampsia. Pre-eclampsia is thought to arise from a combination of impaired placental development and endothelial dysfunction, which leads to hypertension and poor placental perfusion. Fatty acids, through their role in modulating inflammatory pathways and vascular function, may influence these processes [1].

Mendelian randomization leverages genetic variants, typically Single-Nucleotide Polymorphisms (SNPs), which are associated with an exposure of interest, to explore the causal relationship between that exposure and an outcome. Because genetic variants are randomly inherited from parents, they are less likely to be influenced by confounding factors or reverse causality, which can confound observational studies. This makes MR an ideal tool for investigating causal relationships in complex diseases like pre-eclampsia. In the case of plasma fatty acids, genetic variants that affect enzymes involved in fatty acid synthesis and metabolism, such as FADS1 and FADS2, have been identified. These variants can be used as instruments in MR to assess whether changes in fatty acid levels, particularly omega-3 and omega-6 fatty acids, are causally related to pre-eclampsia. Furthermore, MR can be used to examine the reverse relationship—whether pre-eclampsia itself, through physiological changes such as altered lipid metabolism, leads to changes in fatty acid profiles [2].

Using MR, researchers can test whether plasma fatty acids have a direct causal effect on the development of pre-eclampsia. Several studies have focused on omega-3 fatty acids, which are known to have anti-inflammatory and anti-thrombotic effects, both of which are beneficial in preventing pre-eclampsia. For instance, genetic variants in the FADS1 and FADS2 genes, which are involved in the synthesis of long-chain polyunsaturated fatty acids (such as DHA and EPA), have been associated with higher levels of omega-3 fatty acids. MR studies using these variants as instruments could help clarify whether higher levels of omega-3 fatty acids reduce the risk of developing pre-eclampsia. Conversely, omega-6 fatty acids, which are often found in processed foods and vegetable oils, may promote pro-inflammatory pathways that contribute to endothelial dysfunction and hypertension, which are hallmarks of pre-eclampsia. Genetic variants influencing omega-6 fatty acid metabolism can also be used in MR to test whether higher omega-6 levels increase the risk of pre-eclampsia [3].

The second aspect of bidirectional MR is the possibility that pre-eclampsia itself might influence plasma fatty acid levels. Women with pre-eclampsia often experience altered lipid metabolism, including increased triglycerides and changes in the fatty acid composition of plasma lipids. This raises the question of whether pre-eclampsia leads to changes in fatty acid metabolism that could further affect maternal health and pregnancy outcomes. By applying BMR, researchers can test whether the metabolic changes associated with pre-eclampsia cause subsequent alterations in fatty acid profiles.

This reverse causality is important because if pre-eclampsia is shown to alter fatty acid metabolism, it would suggest that interventions aimed at modulating fatty acid levels during pregnancy might not only prevent pre-eclampsia but could also be useful in managing its progression. Recent studies using MR have provided some evidence supporting a potential causal link between omega-3 fatty acids and a reduced risk of pre-eclampsia. However, the evidence is still evolving, and more robust studies using bidirectional MR are needed to clarify the relationship. It is also essential to consider the influence of genetic heterogeneity, as different populations may exhibit varying responses to fatty acid metabolism based on genetic backgrounds. In the

***Address for Correspondence:** Genine Huang, Department of Clinical Laboratory, Obstetrics and Gynecology Hospital of Fudan University, Shanghai 200090, China, E-mail: genin@edu.cn*

Received: 29 January, 2025, Manuscript No. hgec-25-164247; **Editor Assigned:** 31 January, 2025, PreQC No. P-164247; **Reviewed:** 14 February, 2025, QC No. Q-164247; **Revised:** 19 February, 2025, Manuscript No. R-164247; **Published:** 26 February, 2025, DOI: 10.37421/2161-0436.2025.16.274

future, large-scale genomic studies that integrate MR with detailed clinical data on pre-eclampsia outcomes will help refine our understanding of how fatty acids influence pre-eclampsia risk [4].

The identification of specific genetic mutations can open the door to targeted therapies, which are designed to address the underlying genetic defect. For example, in Spinocerebellar Ataxia (SCA), gene therapy and small molecule drugs that target the genetic mutations are being explored as potential treatments. By understanding the exact genetic mutation causing the disorder, researchers can focus on developing drugs that target the molecular mechanisms involved. In Parkinson's disease, genetic discoveries have led to the development of targeted treatments aimed at specific mutations, such as those involving the LRRK2 gene. Clinical trials are currently investigating inhibitors of the LRRK2 protein as potential therapies to slow the progression of the disease in genetically predisposed patients [5].

Conclusion

Bidirectional Mendelian randomization is a powerful tool for investigating the causal relationship between plasma fatty acids and pre-eclampsia risk. By leveraging genetic variants that influence fatty acid metabolism, researchers can uncover whether fatty acids directly influence the risk of pre-eclampsia or whether the disease itself leads to changes in fatty acid profiles. As this field develops, it holds promise for providing clearer guidance on dietary interventions and therapeutic strategies that could reduce the burden of pre-eclampsia, improving outcomes for both mothers and babies.

Acknowledgment

None.

Conflict of Interest

There are no conflicts of interest by author.

References

1. Marschner, Simone, Amy Von Huben, Sarah Zaman and Harmony R. Reynolds, et al. "Pregnancy-related cardiovascular conditions and outcomes in a United States Medicaid population." *Heart* 108 (2022): 1524-1529.

2. Khaire, Amrita A., Shivani R. Thakar, Girija N. Wagh and Sadhana R. Joshi. "Placental lipid metabolism in preeclampsia." *J Hypertension* 39 (2021): 127-134.

3. Tyrmi, Jaakko S., Tea Kaartokallio, A. Inkeri Lokki and Tiina Jääskeläinen, et al. "Genetic risk factors associated with preeclampsia and hypertensive disorders of pregnancy." *JAMA cardiol* 8 (2023): 674-683.

4. Julkunen, Heli, Anna Cichońska, P. Eline Slagboom and Peter Würtz, et al. "Metabolic biomarker profiling for identification of susceptibility to severe pneumonia and COVID-19 in the general population." *Elife* 10 (2021): e63033.

5. Hemani, Gibran, Jie Zheng, Benjamin Elsworth and Kaitlin H. Wade, et al. "The MR-Base platform supports systematic causal inference across the human phenome." *elife 7* (2018): e34408.

How to cite this article: Huang, Genine. "Bidirectional Mendelian Randomization Analysis of Plasma Fatty Acids and their Role in Pre-eclampsia Risk." *Human Genet Embryol* 16 (2025): 274.