Multiomics integration of gut microbiota and metabolomics in metabolic dysfunction-associated fatty liver disease (MAFLD) in the elderly: A systematic review proposal

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ABSTRACT

Introduction: Metabolic dysfunction-associated fatty liver disease (MAFLD) has emerged as a major global health concern, particularly among the elderly, who are disproportionately affected due to age-related metabolic changes, immune senescence, and increased vulnerability to chronic diseases. The pathogenesis of MAFLD is multifactorial, involving complex interactions between host genetics, lifestyle factors, and the gut microbiota. The gut-liver axis plays a central role in disease progression, with microbial metabolites influencing hepatic lipid metabolism, inflammation, and fibrosis. Recent advances in multiomics technologies, especially the integration of gut microbiota profiling and metabolomics offer unprecedented insights into these interactions, enabling the identification of novel biomarkers and therapeutic targets. This systematic review aims to synthesise current evidence on the integration of gut microbiota and metabolomics in understanding the progression of MAFLD in elderly populations. Specifically, it seeks to identify microbial and metabolic signatures associated with disease severity, evaluate the methodological quality of multiomics studies, and explore the potential of these approaches for precision diagnostics and personalised interventions. **Materials and Methods:** The review will be conducted in accordance with PRISMA guidelines. A comprehensive literature search will be performed across major databases including PubMed, Scopus, Web of Science, and Embase. Eligible studies will include original research involving elderly individuals (≥60 years) diagnosed with MAFLD, employing multiomics approaches that combine gut microbiota analysis (e.g., 16*S* rRNA sequencing, metagenomics) and metabolomics (e.g., LC-MS, NMR spectroscopy). Data extraction will focus on study design, population characteristics, omics platforms used, key findings, and limitations. A qualitative synthesis will be conducted to map the current landscape of multiomics research in this domain, and a meta-analysis will be performed where data homogeneity permits. **Results:** The review is expected to provide a comprehensive overview of gut microbial and metabolic alterations associated with MAFLD progression in the elderly. It will highlight consistent patterns across studies, such as shifts in microbial diversity, enrichment of pro-inflammatory taxa, and changes in metabolite profiles linked to lipid metabolism and oxidative stress. The review will also identify gaps in current research, including underrepresentation of elderly cohorts, variability in omics methodologies, and lack of longitudinal data. These findings will inform future research directions and support the development of age-specific diagnostic and therapeutic strategies. **Conclusion:** As the global population ages, understanding the unique pathophysiological mechanisms of MAFLD in elderly individuals becomes increasingly important. Multiomics integration represents a powerful tool to unravel the complexity of the gut-liver axis and its role in disease progression. This systematic review will contribute to the growing body of knowledge in precision hepatology, offering insights that could lead to earlier diagnosis, improved risk stratification, and targeted interventions tailored to the aging population. Ultimately, it aims to bridge the gap between omics research and clinical application, fostering a more personalised approach to managing MAFLD in the elderly.

Keywords: MAFLD, multiomics, metabolomics, gut microbiota, elderly