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Gut microbiome alteration in HIV/AIDS and the role of an-tiretroviral therapy – a scoping review protocol

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Retrospective register of the scoping review. The review is currently undergoing peer review.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 October 2024 and was last updated on 10 October 2024.

INTRODUCTION

Review question / Objective Our aim was to conduct a scoping review on the shifts in the gut microbiota follow-ing HIV/AIDS, particularly in association with the initiation of antiretroviral therapy.
Three key research questions are addressed in this scoping review:
1. Mapping the gut microbiome in adult patients with HIV, who are receiving integrase strand transfer inhibitor-based therapy compared to HIV infected ART naïve patients.
2. Mapping the gut microbiome in adult patients with HIV, who are receiving a non-nucleoside reverse transcriptase inhibitor-based regimen compared to HIV infected ART naïve patients.
3. Mapping the gut microbiome in adult patients with HIV, who are receiving integrase strand transfer inhibitor-based therapy compared to those on a non-nucleoside reverse transcriptase inhibitor-based regimen.

Background The gut microbiota is a complex ecosystem comprising 10 to 100 trillion bacterial cells, fungi, and viruses. Its functionality and communication with the host are supported by a network of metabolomic and proteomic interactions. However, both HIV infection and antiretroviral therapy (ART) can significantly alter its composition. HIV infection results in the depletion of CD4 T-cells within gut-associated lymphoid tissue (GALT), a critical site for HIV replication during the acute phase of infection and the primary location of CD4 T-cell loss. This immune disruption compromises the integrity of the intestinal barrier, allowing the translocation of microbiota and their components into the systemic circulation. Increased intestinal permeability triggers immune responses and initiates systemic inflammation.

Chronic immune activation has been associated with the progression to acquired immune deficiency syndrome (AIDS), the development of non-AIDS-related comorbidities, and increased mortality in HIV-infected individuals. Current guidelines recommend the immediate initiation of ART following HIV diagnosis to restore immune function and increase CD4 counts. The gut microbiota's role in HIV infection has become an increasingly important area of research. However, the effects of ART on the gut microbiome remain relatively underexplored.

Rationale This scoping review aims to compare the impact of integrase strand transfer inhibitors (INSTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs) on the gut microbiota of individuals living with HIV.

METHODS

Strategy of data synthesis Systematic literature searches were conducted in PubMed and Web of Science from their inception, without applying any language or publication filters. Both Medical Subject Headings (MeSH) and free-text keywords were used to ensure a thorough search. Included terms were: HIV, acquired immunodeficiency syndrome, human immunodeficiency virus, AIDS, opportunistic infections, PLHIV, AIDS-related opportunistic infections, acquired immunodeficiency syndrome, gastrointestinal microbiome, microbiome, gut microbiome, gut dysbiosis, metagenomics, microbiota.

Eligibility criteria This study aims to investigate the effects of various antiretroviral therapy (ART) regimens on the gut microbiota and metabolome in adults diagnosed with HIV, confirmed through serological testing. The analysis is based on three comparisons. First, we will assess a population of HIV-infected adults receiving ART based on integrase strand transfer inhibitors (INSTIs) compared to ART-naïve patients, with the primary outcome being alterations in the gut microbiome and metabolome (PICO 1). Second, the study will evaluate HIV-infected adults treated with ART based on non-nucleoside reverse transcriptase inhibitors (NNRTIs) in comparison to ART-naïve individuals, again focusing on changes in the gut microbiome and metabolome (PICO 2). Finally, the third comparison will explore the differences between ART regimens, specifically comparing patients receiving INSTI-based ART with those on NNRTI-based ART, examining gut microbiome and metabolome alterations between these two treatment groups (PICO 3). For all three PICOs, studies written in English were considered if they fell into the following categories: reviews, randomized controlled trials, single-arm trials, cohort stud-ies, and case-control studies. The following types of publications were excluded: case se-ries, case reports, clinical guidelines, non-peer-reviewed literature, conference abstracts, letters, and editorials.

Source of evidence screening and selection Systematic literature searches were conducted in PubMed and Web of Science from their inception, without applying any language or publication filters. Both Medical Subject Headings (MeSH) and free-text keywords were used to ensure a thorough search. The search strategy was tested against eight preselected studies known to be relevant and was validated accordingly. Additionally, reference lists of relevant systematic reviews were manually searched to identify any further eligible studies. Study selection took place in two stages: 1) screening of titles and abstracts, and 2) full text review. Both stages were conducted by a single reviewer using Excel (version 2013). As a limitation of our scoping review there was only one reviewer for the literature data collection.

Data management One reviewer extracted the data from the selected studies, which included study title, authors, study design, participant characteristics, details of the intervention, follow-up duration, and key outcomes (alpha diversity, beta diversity, main changes in bacterial composition, markers of bacterial translocation or systematic inflammation). The results were synthesized and displayed through tables and figures to provide a clear overview of the existing research in this area, as well as to identify any potential research gaps. As this is a scoping review, a formal risk of bias assessment was not performed.

Language restriction English.

Country(ies) involved Hungary.

Keywords AIDS; acquired immunodeficiency syndrome; HIV; human immunodeficiency virus; microbiome; dysbiosis; microbiota; metagenomics; non-nucleoside reverse transcriptase inhibitor; integrase strand transfer inhibitors.

Contributions of each author

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