

Diabetes and HIV: Protocol for a Systematic Review

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Protocol

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Abstract

Background: The HIV/AIDS challenge continues to affect millions of people worldwide. Over 77 million cases of people infected have been recorded and over 35 million of these have died. Due to availability of effective anti-retroviral therapy in the recent years, mortality due to AID-related illness has been declining; resulting in PLWH living longer. This increase in longevity, along with the adverse effects of some anti-retroviral medications has led to an increase in developing chronic diseases that are age-related, such as diabetes among PLWHIV. This makes it important to embark on a systematic review of literatures to establish the magnitude and the impact of diabetes in PLWH, hence this study.

Method: Guided by the PRISMA-P 2015 checklist, a mapping of evidence from studies that are related in peer-reviewed journals that were published from 2000 to 2019 globally will be done. An electronic keyword search of Pubmed, Medline, PsycInfo and EMBASE databases will be carried out. A title screening will be followed by an independent screening of the abstracts and full texts by two reviewers. Any study that is concerned with the prevalence and/or incidence of diabetes among adults (18 years or older) persons living with HIV (PLWH), risk factors of diabetes among PLWH will also be considered. The data will be analyzed using the meta () command R software version 3.6.1

Discussion: This review will chart an evidence in the literature of prevalence and incidence of diabetes among PLWH, risk factors of diabetes among PLWH and compare it with the prevalence, incidence and risk factors of diabetes among the general populace.

Background

The HIV/AIDS scourge is a significant health challenge of the 21st century that keeps on affecting large population worldwide. Since the inception of the scourge over 77 million people have been infected with HIV, with over 35 million death as at 2017 out of which about 1 million was in 2017 alone^{1,2}

Close to 1 million of an approximate 37 million people living with HIV in 2017 globally did not know they were positive^{1,2}

However, mortality due to AIDS-related illnesses has been declining due to reasons such as increase in awareness of HIV status, early initiation of therapy, more effective antiretroviral (ARV) therapy among others^{1,2}

With adherence to medications, life expectancy of people living with HIV (PLWH) has improved since the advent of the combination antiretroviral therapy; equivalent to the general population's estimated lifespan into the early seventies^{3,4,5}.

Nevertheless, longer life spans have led to the emergence of many chronic medical problems in PLWH^{6,7,8,9}

One of the chronic comorbidities in PLWH is diabetes mellitus. Diabetes, is a chronic condition that occurs when there are raised levels of glucose in the blood because the body cannot produce any or enough of the hormone insulin or use insulin effectively.¹⁰

The body's pancreas gland produces the important hormone, insulin, which carries glucose from the blood stream into the cells of the body. Here, glucose is transformed into energy. When insulin is lacking or when the cells are unable to respond to insulin, the result is high blood glucose levels, or hyperglycaemia, which is diabetes hallmark. The long-term effect of hyperglycaemia can lead to damage to different body organs and cause debilitating and grave health complications. Some common complications include cardiovascular disease, nephropathy, neuropathy, and eye disease that may result to retinopathy and blindness. Nonetheless, these complications can be postponed or reversed if diabetes is managed properly.

In addition to type 1, type 2 and gestational diabetes, which are the main types, secondary diabetes develops as a complication of other diseases; for instance, Pancreatitis and hormonal disorders such as Cushing's disease.¹¹ Factors associated with diabetes progression in PLWH are similar with that of people without HIV; they include older age, descent, higher BMI, higher triglyceride, lower total cholesterol, hypertension. PLWH, however, have additional risk factors of HIV and HIV treatment.^{12,13,14} Nucleoside reverse transcriptase inhibitors and protease inhibitors (PIs) are antiretroviral medications that have been implicated in causing metabolic disorders such as insulin resistance, hyperglycaemia and diabetes.^{13,15}

Nonetheless, findings differ across different studies as to whether HIV or ARVs results in increased incidence and prevalence of diabetes, therefore it is imperative to have a systematic review of these studies in order to arrive at a scientifically sound conclusion that could make decision making easier for clinicians.

Because diabetes has effect on the immune system and several body organs leading to disabilities and death if not detected early and properly managed and could affect the outcome of HIV treatment/management, understanding its prevalence and risk factors in PLWH can assist clinicians assess, detect and manage diabetes early enough to prevent complications, fatalities as well as improve the outcome of HIV treatment/management.

This review aims to determine the incidence/prevalence of diabetes as well as the risk factors for diabetes amongst persons living with HIV. To achieve that end, this proposed systematic review will answer the following questions:

1. What is the prevalence of diabetes amongst persons living with HIV (PLWH)?
2. What is the incidence of diabetes among PLWH?
3. What are the risk factors for diabetes among PLWH?
4. Is the prevalence of diabetes among PLWH higher than that of the general populace?

5. Is there difference in risk factors for diabetes among PLWH and the general population?

Method/design

Method/Design

Systematic review framework

The protocol for this systematic review is founded on the PRISMA-P 2015 checklist (Moher et al, 2015).¹⁶ The systematic review will rely on the PRISMA guideline for systematic review (Moher, Liberati, Tetzlaff, Altman, & the PRISMA Group, 2009).¹⁷

Eligibility criteria

Studies will be included based on the following outlined criteria:

Study designs

We will include cross-sectional studies and cohort studies. Studies must have been published in peer-reviewed journals, in English language or in any other language but translated into English language by Google translator.

Participants

We will include studies that examined the prevalence and/or incidence of diabetes among adult (18 years or older) persons living with HIV (PLWH), risk factors of diabetes among persons living with HIV. We will exclude studies that examined persons less than 18 years of age or pregnant women.

Interventions or Concepts

Interventions or concepts of interest are, prevalence of diabetes, incidence of diabetes, risk factors of diabetes among persons living with HIV and associations between HIV infection/use of anti-retroviral therapy and prevalence of diabetes.

Comparators

1. Prevalence of diabetes among the general populace will be compared with prevalence of diabetes among persons living with HIV of same gender and age brackets
2. Risk factors for diabetes among general population will be compared with risk factors for diabetes among persons living with HIV of same gender and age brackets.

Timing

We will select and include studies based on how long the participant tested positive for HIV and how long has how long the participant has been of ARVs as follows:

1. For the comparator group, participant must have tested positive for HIV for at least 1 year.
2. For the study group, participant must be on ARVs for a minimum of 1 year

Setting

There will be no restriction by type of location or country of study. Therefore, studies from all settings will be included as long as such studies have met the inclusion criteria.

Language

We will include articles reported in English language and articles reported in any other language but can be translated into English language by google translator.

Information

Literature search approaches will be developed with medical subject headings (MeSH) and text words related HIV, diabetes, prevalence and risk factors. We will explore Pubmed, Medline, PsycInfo and EMBASE for articles to be included in the systematic review. Also manual searches will be conducted. Reference lists of incorporated studies or related reviews identified during the search will be examined to ensure literature saturation. We will also search the personal files of the authors in order to ensure that all relevant material has been incorporated. The dates for all searches will be noted and included in reporting the review. All literature searches will be done in English language but any relevant study in any language obtained from the searches that provided an option to be translated into English language will also be included. We will also contact authors of included studies in some clarification or additional information is required.

Search strategy

Draft Pubmed search

PubMed database will be searched for articles to identify relevant studies. Terms that will be used in differing combinations to locate a comprehensive list of articles are: HIV, HIV/AIDS, AIDS, Human Immunodeficiency Virus, Acquired immunodeficiency Syndrome, Diabetes, hyperglycemia, endocrine system disease, metabolic disease, glucose intolerance, diabetes mellitus, type 2 diabetes, type 1 diabetes, drug induced diabetes, prevalence, epidemiology, and incidence. Boolean operators AND as well as OR will be used for the database.

Study records

Data management

Results of literature searches will be uploaded to Distiller Systematic Review (DSR) software or Eppi reviewer, depending on which one the reviewers are familiar with (these are internet based software programmes), to facilitate collaboration among reviewers during study selection procedure. The reviewers

will work together to build up, test, pilot and refine the screening questions and form for evaluations based on the inclusion and exclusion criteria. Citation abstracts and full text articles will be uploaded along with screening questions to DRS or Eppi reviewer as preferred by the reviewers. To avoid including duplicate publications, studies will be arranged based on authors and remove duplicate publications.

Selection process:

The reviewers will carry out an independent screening of the titles and abstracts that are obtained from the search against the inclusion criteria of the systematic review. We will acquire full texts for all titles that appear to meet the inclusion criteria or where there is any form of ambiguity. Reviewers will then conduct an independent screening of the full text reports and decide if these conform to the inclusion criteria. We will seek further data from study authors where required, to answer questions about eligibility. We will resolve discrepancies through deliberations; conclusions will be drawn based on the positions of the majority of the reviewers. We will document the basis for excluding studies. We will then measure the quality of every study that met the inclusion criteria as explained, with the use of the quality assessment tool for observational cohort and cross-sectional studies as developed by the National Heart, Lung, and Blood Institute (2014); which consists of 14 yes/no questions. After that data will be obtained from all the studies that passed the quality assessment test.

Data collection process:

We will extract the following data into a table using Microsoft Word (Microsoft Corporation, Redmond, WA), the title of the study, the author(s), the study design, the purpose of the study, sample size, the study setting, mean age of the study sample, gender distribution, prevalence of diabetes, incidence of diabetes and risk factors of diabetes. Data fields in the table will include 'title and author(s)', 'design and purpose', 'sample and setting', this will include the sample size, mean age, gender distribution and study setting, 'prevalence/incidence of diabetes in PLWH', and 'risk factors for diabetes in PLWH'. This process will be done independently by each reviewer.

Data items

We obtain the following information from included studies: The journal where study was published (only studies published in pair reviewed journals will be included), the title of the study, the author(s), the study design (only cohort and cross sectional studies will be included), the purpose of the study, sample size, the study setting, mean age of the study sample, gender distribution, prevalence of diabetes, incidence of diabetes and risk factors of diabetes.

Outcome Prioritization

Primary outcomes:

Prevalence of diabetes amongst persons living with HIV

Incidence of diabetes amongst persons living with HIV

Risk factors of diabetes amongst persons living with diabetes

Secondary outcomes:

Association between HIV and incidence/prevalence of diabetes

Association between HIV and anti-retroviral therapy

Risk of bias of individual studies

To evaluate the risk of bias in included cohort and cross sectional studies, the procedural worth of potential studies will be assessed with the use of the Newcastle-Ottawa scale (NOS) for measuring the quality of non-randomized studies in meta-analyses. The NOS for cohort studies will be modified to meet the precise needs of this systematic review. Using the NOS, for each study, at least one star will be accorded to each numbered item in the 'Selection' and 'Outcome' categories. A maximum of two stars can be allotted for 'Comparability'. Hence studies will be accorded a maximum of nine points on items associated with the selection of study groups; the comparability of the groups, and the determination of end result of interest. This will be carried out by two discrete reviewers. A third reviewer will serve as an arbitrator where there is contention.

Data synthesis

If the studies are adequately compatible with respect to design, age profile of sample population and sufficiently large enough sample size, we will conduct meta-analysis using Forest plot.

We will test clinical discrepancy by assessing the variability in participants' age and gender in the included studies. Chi-square test will be used to test statistical heterogeneity, significance level will be kept at 0.5.

If substantial discrepancy exists, we would not carry out a meta-analysis; a qualitative narrative, survey will be done.

A systematic narrative synthesis will be done using tables and texts to summarise and explain the characteristics and findings both inside and between included studies, in accordance with the guidance from the Centre for Review and Dissemination.

Meta-bias(es)

Meta () command in R software version 3.6.1 will be used to assess bias in and across studies using Funnel plot

Confidence in cumulative estimate

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) will be used to appraise the evidence for all outcomes. The merit of evidence will be rated across the domains of risk of bias, consistency, directness and accuracy as well as publication bias.

Declarations

Ethics approval and consent to participate: Not applicable

Consent for publication: Not applicable

Competing interests: There is no competing interest

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Authors' contributions: DMU (guarantor of the review), initiated, searched for information and wrote protocol.

PN, supervised the preparation of the protocol and reviewed the protocol.

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Abbreviations

1. AIDS: Acquired Immune Deficiency Syndrome
2. DSR: Distiller Systematic Review
3. Eppi reviewer:
4. HIV: Human Immunodeficiency Virus
5. NOS: Newcastle-Ottawa Scale
6. PLWH: People Living With HIV
7. PRISMA: Preferred Reporting Items for Systematic Reviews
8. PRISMA-P: Preferred Reporting Items for Systematic Review Protocols
9. SPSS: Statistical Package for Social Sciences
10. UNAIDS: The Joint United Nations Programme on HIV and AIDS

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Supplementary Files

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