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Kidney dysfunction and associated factors among adults living with human immunodeficiency virus in Africa: a systematic review and meta-analysis

Worku Chekol Tassew[1*], Agerie Mengistie Zeleke[2], Yeshiwas Ayale Ferede[3] and Girum Meseret Ayenew[4]

Abstract

Background Kidney dysfunction among adults living with Human Immuno-Deficiency Virus (HIV) increases the risk of drug-related side effects, acute kidney injury, hospitalization, and progression to end-stage kidney disease. In developing regions like Africa, where access to kidney transplants and dialysis is limited, early detection of kidney disease among adults living with HIV has significant clinical and financial implications. Therefore, the objective of this review was to determine the pooled prevalence and identify associated factors of kidney dysfunction among adults living with HIV in Africa.

Methods The report was presented according to the Preferred Reporting Items for Systematic Review and Meta-Analyses checklists. The articles were searched using PubMed/MEDLINE, EMBASE, Scopus, Wiley Online Library, CINAHL/EBSCO, OVID/Wolters Kluwer, Cochrane Library, Google Scholar, Science Direct, and African Journal Online. Data were extracted using Microsoft Excel and exported to STATA MP Version 11 Software for analysis. Heterogeneity of studies was assessed by Cochran's Q test and I^2 statistics. Publication bias was detected by the visual inspection of the funnel plot and statistical Egger's test.

Results In this study, the pooled prevalence of kidney dysfunction among adults living with HIV in Africa is estimated to be 16.85% (95% CI: 13.08 – 20.62, I^2=96.2%, p-value = 0.000). Female sex (POR = 1.82; 95% CI; 1.31, 2.53), age ≥ 50 years (POR = 8.94; 95% CI: 1.82, 43.93), body mass index ≥ 30 kg/m^2 (POR = 4.70; 95% CI: 3.07, 7.22), diabetes mellitus (POR = 2.84; 95% CI: 1.59, 5.07), CD4 count < 200 cells/mm^3 (POR = 3.64; 95% CI: 1.63, 8.13) and anemia (POR = 3.73, 95% CI = 2.00–6.94) were factors associated with kidney dysfunction among adults living with HIV.

Conclusions This study revealed that the pooled prevalence of kidney dysfunction among adults living with HIV in Africa remains significant. Female sex, age ≥ 50 years, body mass index ≥ 30 kg/m^2, diabetes mellitus, CD4 count < 200 cells/mm^3 and anemia were factors associated with kidney dysfunction. To reduce the morbidity and mortality associated with kidney dysfunction, it is advisable to create awareness and initiating early interventions through health education during their follow-up time, and initiating suitable medication at an early stage.

*Correspondence:
Worku Chekol Tassew
workukid16@gmail.com

Full list of author information is available at the end of the article

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Introduction

Human immunodeficiency Virus (HIV) is the leading cause of morbidity and mortality especially in Africa [1]. By 2018, the global number of people living with HIV (PLWHIV) was estimated to be around 37.9 million, with 20.6 million of those individuals residing in Eastern and Southern Africa [2]. HIV affects every organ system in the body by direct damage or by rendering the host susceptible to opportunistic infections [3]. The kidneys are one of the most frequently affected sites of infection in individuals with HIV [4]. Impairment of kidney function is the most frequent complication of HIV infection both before and after the introduction of antiretroviral therapy (ART). It is associated with a greater risk of HIV progression and cardiovascular disease [5–8]. It also results in negative outcomes, such as a higher risk of morbidity and mortality [9].

Kidney involvement is commonly observed during HIV infection and has become the fourth leading cause of mortality among individuals who have progressed to acquired immunodeficiency syndrome (AIDS), following sepsis, pneumonia, and liver disease [10]. Kidney dysfunction can arise from various mechanisms, including direct HIV infection, inflammation caused by HIV, comorbid conditions, and medications such as ART [11, 12] and HIV replication in renal cells that damage the kidney [13]. This may also result from frequent complications of the disease, such as dehydration and sepsis, or from the effects of nephrotoxic medications commonly used in the treatment of AIDS [14]. Kidney disease can also arise from the direct impact of HIV infection on the kidneys, leading to specific conditions such as HIV-associated nephropathy (HIVAN), immune complex disease in the setting of HIV, or thrombotic micro-angiopathy (TMA) [15]. Despite the fact that ART has decreased HIV associated kidney diseases, the rise in kidney dysfunction cases might be associated to prolonged exposure to potentially nephrotoxic anti-retroviral drugs like tenofovir, ritonavir-boosted atazanavir, and ritonavir-boosted lopinavir [16, 17].

Kidney dysfunction among adults living with HIV increases the risk of drug-related side effects, acute kidney injury, hospitalization, and progression to end-stage kidney disease [18, 19]. Globally, the estimated prevalence of kidney dysfunction among adults living with HIV varies depending on the method used: 6.4% with the Modification of Diet in Renal Disease (MDRD) equation, 4.8% with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, and 12.3% with the Cockcroft-Gault (CG) formula. The extent of kidney dysfunction also differs by region, with rates of 6.5% in North America, 6.2% in South America, and 2.7% in Europe [20]. In Africa the prevalence of kidney dysfunction among PLWHIV has been reported to be notably high, ranging from 25 to 77% [21].

Early detection and consistent monitoring of kidney dysfunction in PLWHIV are crucial for prognosis, adjusting medication dosages, and managing treatment. The World Health Organization (WHO) recommends evaluating creatinine clearance when starting ART [22]. Recent studies have linked ART discontinuation to increased HIV-related mortality rates. This has led to recommendations for increased vigilance regarding nephrotoxicity, including proactive monitoring for risk factors through regular screening and the implementation of preventative strategies to address ART-induced kidney damage and long-term complications such as HIVAN [23]. In resource-limited settings, regular laboratory monitoring may not always be necessary for effective ART treatment decisions. However, the lack of routine testing raises concerns about the risk of undetected HIV-associated kidney dysfunction [21, 24]. In developing regions like Africa, where access to kidney transplants and dialysis is limited, early detection of kidney disease among adults living with HIV has significant clinical and financial implications. Given the high prevalence of HIV with kidney dysfunction before and after ART, and the adoption of the "test-and-treat" approach in Africa, there is a lack of comprehensive information about kidney function in PLWHIV within these resource-limited settings. Therefore, the objective of this review was to determine the pooled prevalence and identify associated factors of kidney dysfunction among adults living with HIV in Africa.

Methods

Study design and protocol registration

This systematic review and meta-analysis was conducted following the protocol that was registered with International Prospective Register of Systematic Reviews (PROSPERO) (Reference number: CRD42024584073). The report was presented according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA-2020) checklists [25] (Additional file 1).

Data sources and searching strategy

The articles were searched PubMed/MEDLINE, EMBASE, Scopus, Wiley Online Library, CINAHL/EBSCO, OVID/Wolters Kluwer, Cochrane Library, Science Direct, Google Scholar, and African Journal Online

Table 1 Example of PubMed search history for prevalence and associated factors of kidney dysfunction among adults living HIV

Search	Search terms	Hits
1	Chronic kidney disease OR Nephropathy OR Chronic renal failure OR Kidney dysfunction OR Proteinuria OR End-stage kidney/renal disease OR Renal insufficiency	3714
2	Human immunodeficiency OR Peoples living with HIV OR HIV/AIDS	1347
3	Determinants OR Associated factors OR Predictors	1329
4	#1, #2 and #3	1306
5	Limits; articles done in humans, published in English language, conducted among adults and free full text	1,222

Table 2 Framework for determining the eligibility of studies

Criteria	Description
Co-condition	Kidney dysfunction
Co-context	Nigeria OR Egypt OR Morocco OR Kenya OR Tanzania OR Ghana OR Malawi OR Burundi OR Comoros OR Djibouti OR Eritrea OR Ethiopia OR Kenya OR Madagascar OR Malawi OR Mauritius OR Mozambique OR Rwanda OR Seychelles OR Somalia OR South Sudan OR Sudan OR Uganda OR Zambia OR Zimbabwe OR South Africa OR Algeria OR DR Congo OR Uganda OR Angola OR Mozambique OR Ivory Coast OR Cameroon OR Niger OR Mali OR Burkina Faso OR Chad OR Liberia OR Senegal OR Guinea OR Benin OR Rwanda OR Tunisia OR Togo OR Libya OR Gambia OR Gabon OR Botswana OR Namibia OR Central Africa
Population	Adults
Exposure	Adults living with HIV
Outcome	Kidney dysfunction

from August 1 to September 25/2024. EndNote X7 reference manager software was used to collect, organize search results, and remove duplicate articles. In the search process, both Medical Subject Headings (MeSH) and plain text terms were utilized for the following keywords: "Chronic kidney disease," "Nephropathy," "Chronic kidney failure," "Kidney dysfunction," "Proteinuria," "End-stage kidney disease," "End-stage renal disease," "Renal insufficiency," "Human immunodeficiency Virus," "Peoples living with HIV/AIDS," "HIV/AIDS," "Determinants," "Associated factors", "Predictors," "Adults," were identified, and search strings were devised across the databases. Two authors (WCT and YAF) screened articles based on their title, abstract, and/or full text, utilizing Boolean operators "AND" and "OR" to combine search terms. Additionally, the snowball technique was employed from references of retrieved articles to identify additional relevant articles. The disagreements between the authors were resolved by group discussion (See Table 1).

The qualifying standards for this review were established using the CoCoPop and PEO framework (Table 2).

Eligibility criteria

This systematic review and meta-analyses included articles that met the following specific inclusion criteria: [1] observational studies such as cross-sectional, and cohort studies that report the prevalence and associated factors of kidney dysfunction among adults living with HIV or the number of adults with HIV who develop kidney dysfunction; Kidney dysfunction was classified according to the National Kidney Foundation clinical practice guideline based on the GFR as determined by Cockcroft-Gault (CG) formula, MDRD or CKD-EPI equation. Accordingly, estimated GFR values 90 ml/min/1.73 m^2, 60–89 ml/min/1.73 m^2, 30–59 ml/min/1.73 m^2,15-29 ml/min/1.73 m^2 and < 15 ml/min/1.73 m^2 was interpreted as normal, mild, moderate, severe, and kidney failure. Kidney dysfunction was defined as eGFR < 60 ml/min [26]; [2] articles conducted in African countries; [3] only articles that had been published; [4] articles published until August 15, 2024; [5] articles published in English; [6] articles that report the prevalence of kidney dysfunction and [7] articles conducted either in community or health facility settings. Articles lacking full text, unpublished studies, low-quality studies, case reports, qualitative studies, conference papers, as well as systematic reviews and meta-analysis were excluded.

Quality assessment

The quality assessment of the included studies was carried out using the Johanna Briggs Institute (JBI) critical appraisal check list which is freely available at https://jbi.global/critical-appraisal-tools [27]. The checklist comprises nine components. The overall methodological quality of the study is determined by the total score (ranging from 0 to 9), categorized as low (0–4), medium (5–6), or high [7–9] quality. Using the tool as a protocol, the authors (YAF and AMZ) used the blinded review approach to assess the quality of the primary articles. The two authors resolved discrepancies with discussion. Those articles, scores 5 or more in JBI criteria were included in the review. Further discrepancies in the quality assessment was resolved through another author (WCT) (Additional file 2).

Data extraction

After identifying articles for inclusion, two independent authors (GMA and WCT) conducted data extraction, using a standardized data abstraction template created in Microsoft Excel. The Joanna Briggs Institute (JBI) tool was used for the data extraction. This tool was devised

to systematically gather essential information from primary studies. The extracted data item includes primary author's name, publication year, country, study design, response rate, sample size, sampling technique, type of Glomerular Filtration Rate (GFR) confirmatory equations used, prevalence of kidney dysfunction and other effect measures. Odds ratio of each variables were extracted from studies to determine factors associated with kidney dysfunction among adults living with HIV. Each variables were associated in more than two primary studies to pool the odds ratio with each corresponding confidence interval.

Statistical analysis

This review primarily analyzed the pooled prevalence of kidney dysfunction among adults living with HIV in Africa after extraction of each prevalence of studies. The secondary outcome of the study was analyzed using odds ratio of factors associated with kidney dysfunction from two or more primary studies. Data were extracted using Microsoft Excel and exported to STATA version 11 (STATA Corp., LLC) software for analysis. Heterogeneity of studies was assessed by Cochran's Q test and I^2 statistics. A p-value less than 0.05 represent the presence of statistically significant heterogeneity among the included studies [28]. Heterogeneity was classified as no (I^2 =0.0%), low (I^2 < 25%), moderate (25% ≤ I^2 ≤ 75%), or high (I^2 > 75%) [29]. Due to the presence of Heterogeneity among the included studies, a random-effects model was employed to estimate the pooled prevalence of kidney dysfunction [30]. Specifically among the methods of random effect, Der-Simonian–Laird random-effects models was used to generate the pooled prevalence of kidney dysfunction [30].

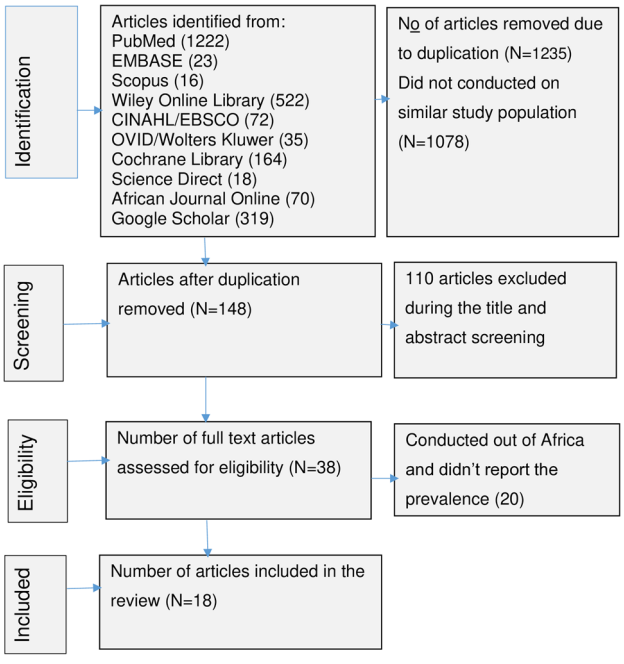

Fig. 1 Flow diagram for the selection of studies included in systematic review and meta-analysis of kidney dysfunction among adults living with HIV in Africa ($n = 18$)

Subgroup analysis

To identify the source of heterogeneity between the included studies, subgroup analysis was done using country, study design, and GFR equation/formula. In addition, meta-regression analysis was conducted using sample size, response rate and publication year as a covariates.

Sensitivity analysis

Sensitivity analysis was also performed to check the effect of each study on the pooled prevalence.

Publication bias

Publication bias was detected by the visual inspection of the funnel plot and statistical Egger's test [31, 32]. A p-value less than 0.05 from Egger's test indicated notable publication bias, implying that studies with larger effects (either positive or negative) are more likely to be published [33]. A trim and fill analysis was performed to address this publication bias [34].

Results

Literature search results

Study selection

The initial search yielded 2,461 primary articles, which were imported into EndNote software version X7 (Thomson Reuters, New York, NY). Of these, 1,222 studies were retrieved from PubMed, EMBASE (23), Scopus (16), Wiley Online Library (522), CINAHL/EBSCO (72), OVID/Wolters Kluwer (35), Cochrane Library (164), Science Direct (18), African Journal Online (70), and Google Scholar (319). Approximately 1235 duplicate articles were removed, along with an additional 1078 articles were excluded as they did not conducted on similar study population. The full texts of the remaining 38 articles were then assessed by two authors (AMZ and YAF) against the eligibility criteria and quality. Additionally, some articles were excluded due to they did not report the outcome of interest or the prevalence of kidney dysfunction. Finally, eighteen (18) studies with total sample size of 7823 focusing on the prevalence of kidney dysfunction were included (Fig. 1).

Overview of included studies

In this systematic review and meta-analysis study, 18 studies were included in eight different African countries. The included studies, published up to August 15, 2024, had a total sample size of 7,823 participants, with individual study sizes ranging from 183 to 1,118 participants.

Five articles were obtained from Ethiopia [35–39], Four were from Tanzania [40–43], two were from Ghana [44, 45], three were from Nigeria [46–48], two were from Zambia [49, 50] and the remaining were from the Uganda and Malawi [51, 52]. All the included articles were published in peer-reviewed journals. Regarding the study design, fourteen studies utilized facility-based cross-sectional study design. The prevalence of kidney dysfunction ranged from 5.5 to 42% (Table 3).

Pooled prevalence of kidney dysfunction

In this study, the pooled prevalence of kidney dysfunction among adults living with HIV in Africa is estimated to be 16.85% (95% CI: 13.08 – 20.62, I^2=96.2%, p-value = 0.000). An I^2 statistic of 96.2% suggests the presence of heterogeneity among the included studies. Due to this heterogeneity, a random-effects model was used to determine the pooled prevalence of kidney dysfunction (Fig. 2).

Subgroup analysis

The subgroup analysis revealed that studies utilizing retrospective cohort showed the highest pooled prevalence of kidney dysfunction among adults living with HIV, which is 22.96% (95% CI: 10.79–35.12, I^2=0%, p-value = 0.8912) (Fig. 3).

The subgroup analysis based on country revealed that the highest pooled prevalence of kidney dysfunction among adults living with HIV were reported from Zambia 24.25% (95% CI: -11.51-60.01, I^2=88.6%, p-value = 0.003) while the least is from Ghana (Fig. 4).

The other subgroup analysis based on diagnostic criteria/method showed that the highest pooled prevalence of kidney dysfunction were found from the study used Cockroft–Gault equation, 25.29% (95% CI: 14.81–35.77, I^2=47.9%, p-value = 0.104) (Fig. 5).

Publication bias

The funnel plot displayed an uneven distribution of studies, suggesting presence of publication bias. This observation was supported by Egger's test, which yielded a statistically significant p-value of 0.000 at the 5% significance level, providing further evidence of publication bias (Fig. 6) (See Table 4).

Trim and fill analysis

To treat the presence of publication bias, trim and fill analysis was carried out, and two iteration cycles were performed, and nine articles were added, making a total of 27 articles with 26 degrees of freedom, a p-value of 0.000, and a moment-based between study variance of 0.631 (Fig. 7).

Meta-regression

We further fitted meta-regression using the random effects model on the aggregated study level variables to address the above heterogeneity. According to the univariable meta-regression analysis, the number of participants, sample size, and publication year were not significant indicating the heterogeneity was not result from these variables (Table 5).

Sensitivity analysis

The subgroup analysis revealed high heterogeneity among the included studies. To evaluate the impact of

Table 3 Overview of included studies in the systematic review and meta-analysis of kidney dysfunction and associated factors among adults living with HIV in Africa (*n* = 18)

Author name	Pub year	Country	Sampling technique	Sample size	Prevalence (%)	Diagnostic criteria
Mekuria et al. [35]	2016	Ethiopia	Consecutive	446	18.2	Cockroft–Gault
Kefeni et al. [36]	2021	Ethiopia	Systematic	359	20.7	CKD-EPI
Fiseha, Gebreweld [37]	2021	Ethiopia	Consecutive	648	22.1	MDRD
Oswin Mwemezi et al. [40]	2020	Tanzania	Simple random	311	7	CKD-EPI
Obirikorang et al. [44]	2014	Ghana	Simple random	163	9.9	MDRD
Mwanjala et al. [41]	2022	Tanzania	stratified sampl	396	20.7	CKD-EPI
Onodugo et al. [46]	2014	Nigeria	Consecutive	300	24.3	Cockroft–Gault
Wondifraw Baynes et al. [38]	2017	Ethiopia	Systematic	275	11.7	MDRD
Obiri-Yeboah et al. [45]	2018	Ghana	Systematic	441	5.2	MDRD
Odongo et al. [51]	2015	Uganda	Consecutive	365	14.4	CKD-EPI
Yilma et al. [39]	2020	Ethiopia	Consecutive	342	26.9	Cockroft–Gault
Kitundu et al. [42]	2024	Tanzania	Consecutive	345	12.1	CKD-EPI
J. Banda et al. [49]	2010	Zambia	Consecutive	302	42	Cockroft–Gault
Agbaji et al. [47]	2007	Nigeria	Simple random	492	23.8	MDRD
Kavishe et al. [43]	2021	Tanzania	Simple random	956	8.1	CKD-EPI
Deckert et al. [50]	2017	Zambia	Simple random	1118	5.5	CKD-EPI
Glaser et al. [52]	2016	Malawi	Consecutive	381	11.2	Cockroft–gault
Adedeji et al. [48]	2015	Nigeria	Consecutive	183	24	MDRD

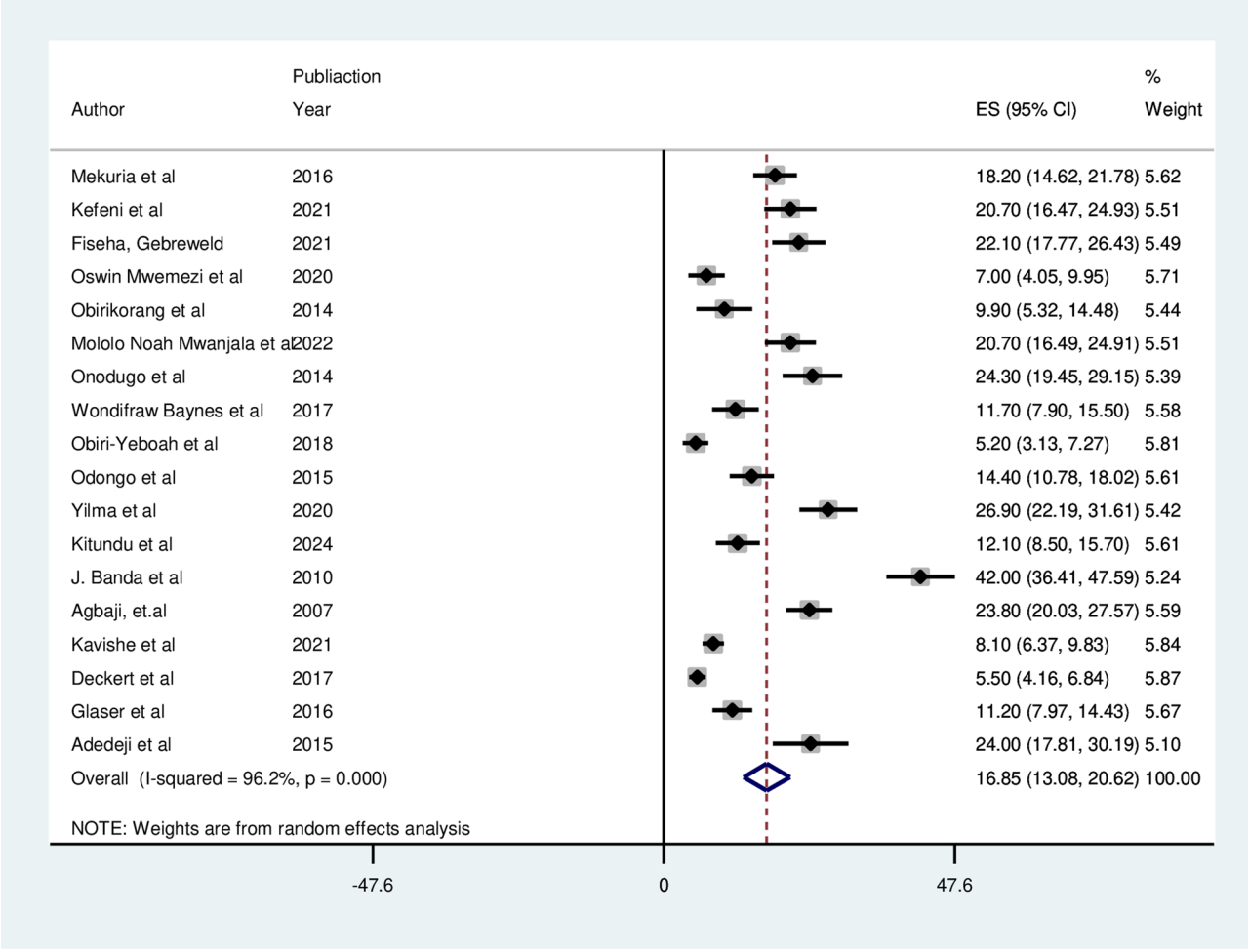

Fig. 2 Forest plot for the pooled prevalence of kidney dysfunction among adults living with HIV in Africa ($n = 18$)

each study on the pooled estimate, a sensitivity analysis was conducted. Based on the analysis, none of the individual primary studies influenced the pooled prevalence of kidney dysfunction.

Factors associated with kidney dysfunction

Based on this meta-analysis, kidney dysfunction was associated with female sex, age ≥ 50 years, CD4 count less than 200 cells/mm^3, Body Mass Index (BMI) ≥ 30 kg/m^2, anemia and diabetes mellitus (DM).

Socio-demographic factors: In the present analysis, the pooled effect of three studies showed that female sex had higher odds of kidney dysfunction (POR = 1.83; 95% CI; 1.31, 2.53) than their counterparts. The result of heterogeneity test (I^2=0.0%) showed the absence of heterogeneity among the included studies. Additionally, the pooled effect of two studies showed that age ≥ 50 years was statistically associated with kidney dysfunction among adults living with HIV (POR = 8.94; 95% CI: 2.82, 43.93). The heterogeneity test (I^2 =94.8%) showed the presence of high heterogeneity between the included studies.

Clinical factors: This study showed that those adults with CD4 count < 200 cells/mm^3 were found to be 3.64 times more likely to develop kidney dysfunction than their counterparts (POR = 3.64; 95% CI: 1.63, 8.13). The heterogeneity test (I^2 =78.1%) showed the presence of high heterogeneity among the included studies. Additionally, adults living with HIV with BMI ≥ 30 kg/m^2 were 4.70 times more likely to develop kidney dysfunction than those with BMI 18.5–24.9 kg/m^2 (POR = 4.70; 95% CI: 3.07, 7.22). The result of heterogeneity test (I^2 =0.0%) showed the absence of heterogeneity between the included studies. Furthermore, adults living with HIV who had anemia were 3.73 times more likely to develop kidney dysfunction compared with adults without anemia (POR = 3.73, 95% CI = 2.00–6.94). The heterogeneity test in this analysis (I^2 =80%) revealed that the presence of high heterogeneity across studies. Finally, the pooled effects of two studies indicated that those adults living with HIV who had DM were 2.84 times more likely

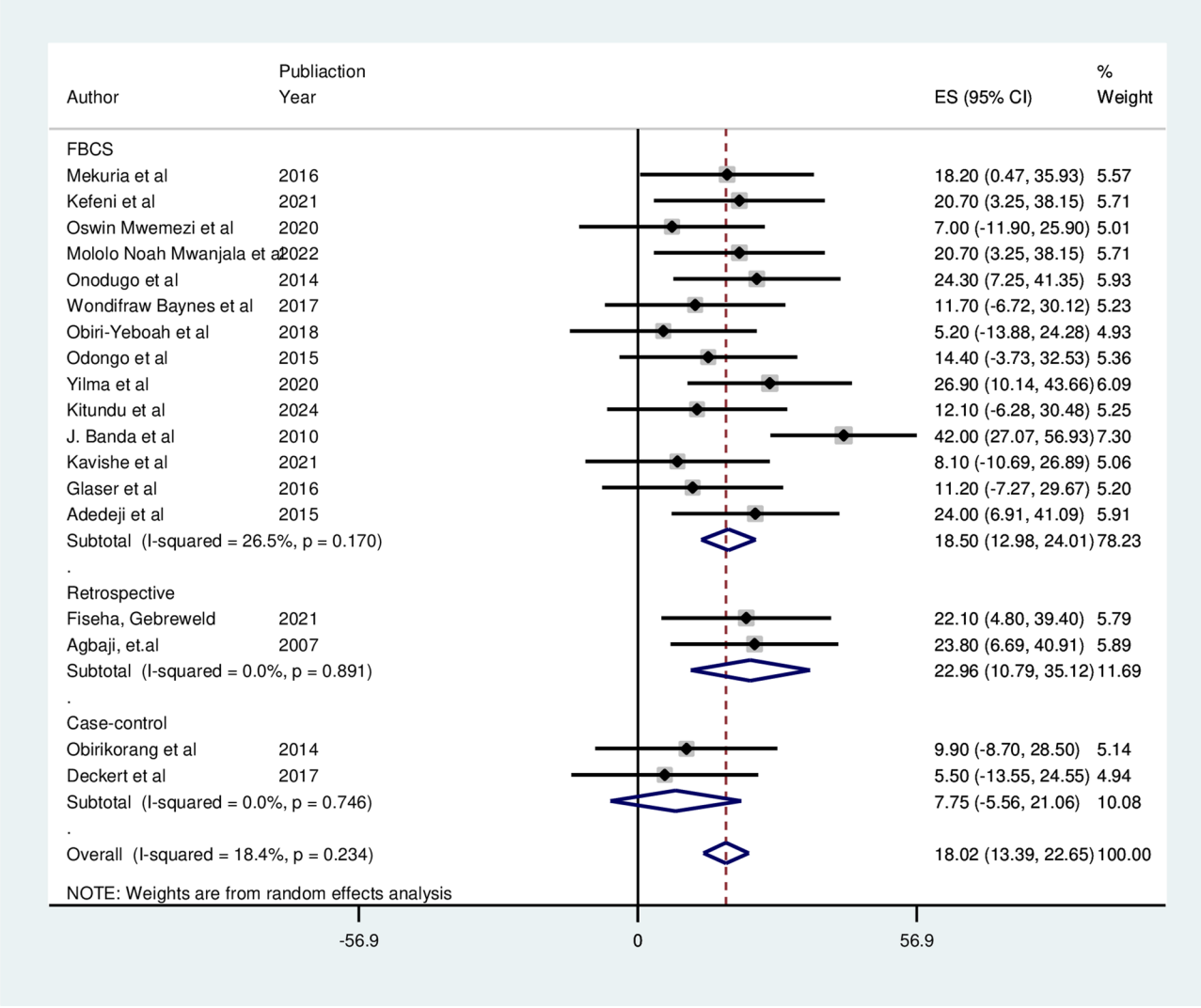

Fig. 3 A subgroup analysis of the forest plot showing the pooled prevalence of kidney dysfunction among adults living with HIV in Africa based on the study design ($n = 18$)

to develop kidney dysfunction than their counterparts (POR = 2.84; 95% CI: 1.59, 5.07). The heterogeneity test (I^2 =52.7%) showed the presence of heterogeneity between the included studies (Fig. 8).

Discussion

In this study, the pooled prevalence of kidney dysfunction among adults living with HIV in Africa is estimated to be 16.85% (95% CI: 13.08 – 20.62, I^2=96.2%, p-value = 0.000). The prevalence of kidney dysfunction (eGFR < 60 ml/min/1.73 m^2) found in this study is higher than that reported in studies from China and Spain [53, 54], which showed rates of 3.3% and 5%, respectively, before ART initiation using the same MDRD formula for eGFR. This difference is likely due to variations in patient characteristics or discrepancies in creatinine assays and calibration methods. Another explanation for this inconsistencies might be due to significant differences in socioeconomic characteristics (limited healthcare infrastructures and poor health care quality and access), lifestyles, systemic challenges and inadequate access to reliable laboratory testing significantly hampers the effective management of HIV-associated kidney dysfunction in resource-limited settings. It suggests that HIV itself contributes to kidney dysfunction, irrespective of the potential nephrotoxic effects of antiretroviral medications. The underlying cause of HIV-related kidney dysfunction is thought to be either direct cellular damage by the virus or changes in cytokine release during HIV infection.

However, findings from studies conducted in Brazil (8%), London (12%), and Turkey (15.7%) report lower prevalence rates of kidney dysfunction [9, 55, 56]. Population variation, study design, sample size, definition used to classify kidney dysfunction, and the use of various

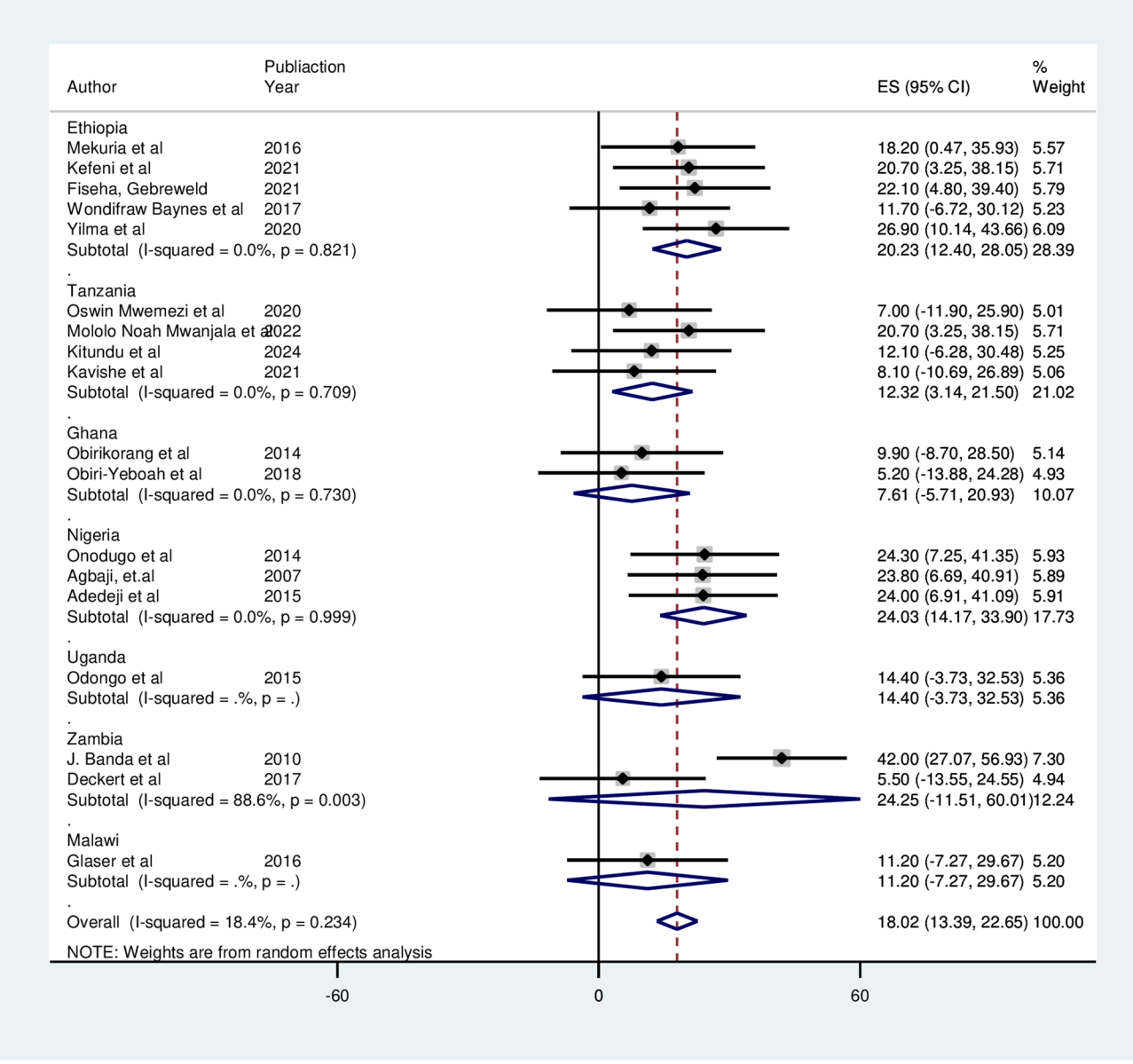

Fig. 4 A subgroup analysis of the forest plot showing the pooled prevalence of kidney dysfunction among adults living with HIV in Africa based on country ($n = 18$)

diagnostic methods (e.g., CKD-EPI, MDRD, Cockcroft-Gault) may contribute to the differences observed. The other interesting reason for the discrepancy is that Intracellular apolipoprotein L1 (APOL1) protein lacking a signal peptide is retained within the cell; it is this protein isoform that leads to kidney injury. The APOL1 renal risk variants are found exclusively on African-derived chromosomes and are not present on European or Asian chromosomes. *APOL1* genetic variants account for much of the excess risk of chronic and end stage kidney disease, which results in a significant global health disparity for persons of African ancestry. We estimate the lifetime risk of kidney disease in APOL1 dual-risk allele individuals to be at least 15%. Experimental evidence suggests a direct role of APOL1 in pore formation, cellular injury, and programmed cell death in renal injury [57]. APOL1- mediated kidney disease (AMKD) is a type of kidney disease caused by variants (changes) in the APOL1 gene. Certain *A*POL1 variants have been linked with different types of kidney disease, including a higher risk of high blood pressure-related chronic kidney disease (CKD) or kidney failure, focal segmental glomerulosclerosis (FSGS), and HIVAN. Variants linked with disease are known as risk variants, such as APOL1 risk variants. Certain APOL1 risk variants have been linked with a higher risk of kidney disease in people of Western and Central African

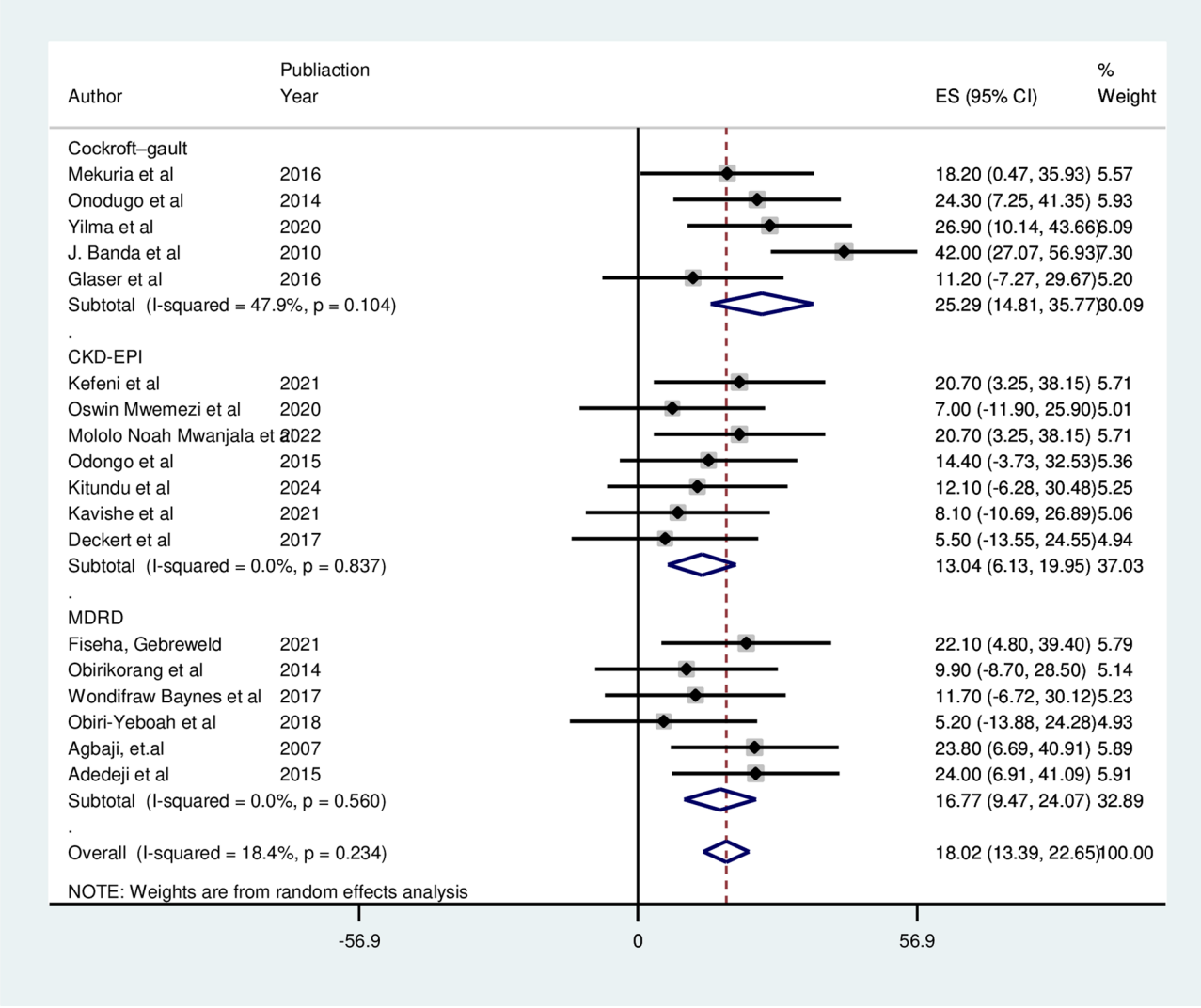

Fig. 5 A subgroup analysis of the forest plot showing the pooled prevalence of kidney dysfunction among adults living with HIV in Africa based on diagnostic criteria ($n = 18$)

descent. Genetic variants in APOL1 are a major contributor to the increased risk of kidney disease in people of recent African ancestry [58].

The findings of this study revealed that advanced age (≥ 55 years) is a risk factor for kidney dysfunction. The findings of the study is supported by the study conducted in Italy [59]. This is because aging significantly impacts the deterioration of renal-vascular function. As people grow older, their blood vessels become stiffer, which can lead to renal vascular issues. Additionally, aging can increase the likelihood of developing various co-morbid conditions due to factors like oxidative stress, cell death, heart deterioration, and degeneration [60, 61]. Aging is a non-modifiable risk factor that played a significant role in the development of kidney dysfunction in the finding of this study, suggesting the need to implement possible preventive measures in these sub-group of population for reducing progression to kidney failure. Therefore, our data remind clinicians to strengthen ART care programs to meet the rising challenge of kidney dysfunction. Additionally, screening among such a highly selected population may help identify those that would most benefit from modifiable factors, including lifestyle changes, associated with the progression of kidney dysfunction, especially in early stages.

Adults living with HIV with BMI ≥ 30 kg/m² were more likely to develop kidney dysfunction than those with BMI 18.5–24.9 kg/m². While the exact mechanisms between obesity and kidney dysfunction are not yet fully understood, there is some evidence suggesting that obesity-induced excessive fat deposition in the kidneys can result in the buildup of harmful metabolites from fatty acid metabolism [62]. Elevated BMI following the start of ART is associated with cardio-metabolic problems, such as

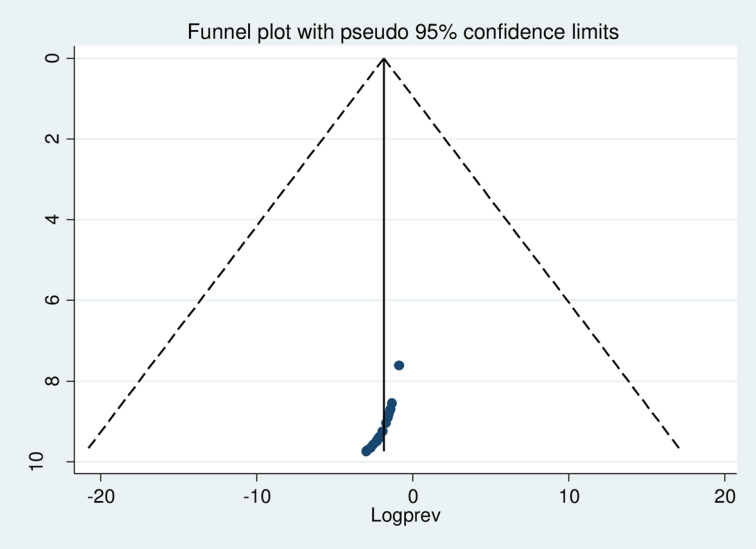

Fig. 6 Funnel plot showing publication bias

Table 4 Egger's regression test assessing publication bias

Std-Eff	Coefficient	Std. Error	*p*-value	95%upper conf. I	95%lower conf. I
Slope	3.82	0.08	0.000	3.65	3.99
Bias	-3.37	0.04	0.000	-3.47	-3.27

Table 5 Univariable meta-regression analysis results for the pooled prevalence of kidney dysfunction in Africa

Study level variables	Coefficients	Standard error	*P*>|t|	[95% CI]
Participants	-0.002	0.03	0.93	(-0.074 – 0.06)
Pub year	-0.05	0.52	0.92	(-1.17–1.06)
Sample size	0.001	0.03	0.95	(-0.06–0.07)

athero-thrombotic cardiovascular disease and diabetes, which can heighten the risk of kidney dysfunction during HIV treatment [1]. Obesity increases tubular reabsorption and this shifts pressure natriuresis towards higher BP. The increased tubular re-absorption is not directly related to hyperinsulinaemia, but is closely linked to activation of the sympathetic and renin-angiotensin systems, and possible changes in intra-renal physical forces caused by medullary compression due to accumulation of

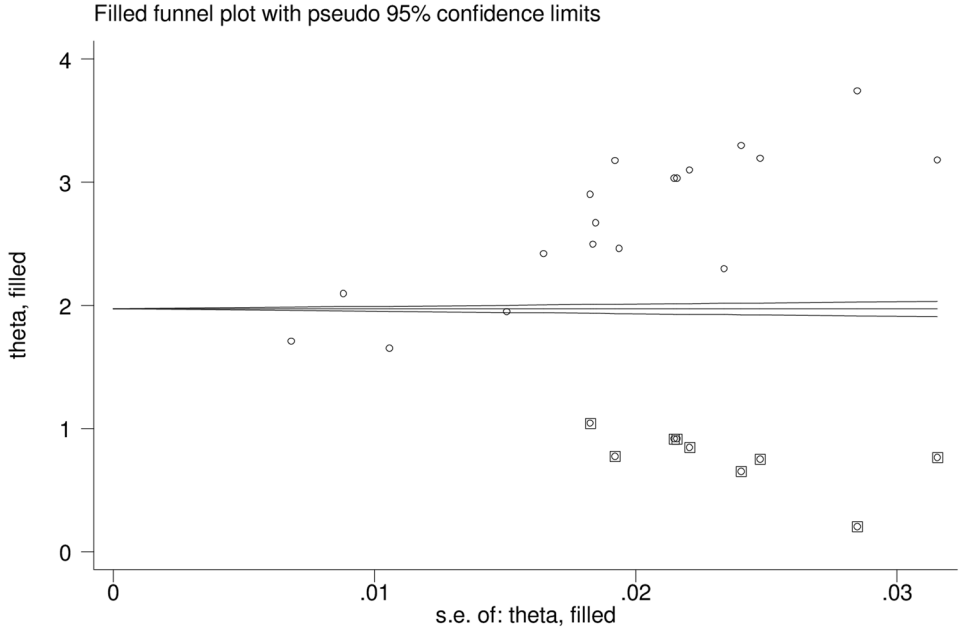

Fig. 7 Trim and fill analysis for the asymmetrical distribution of the included studies

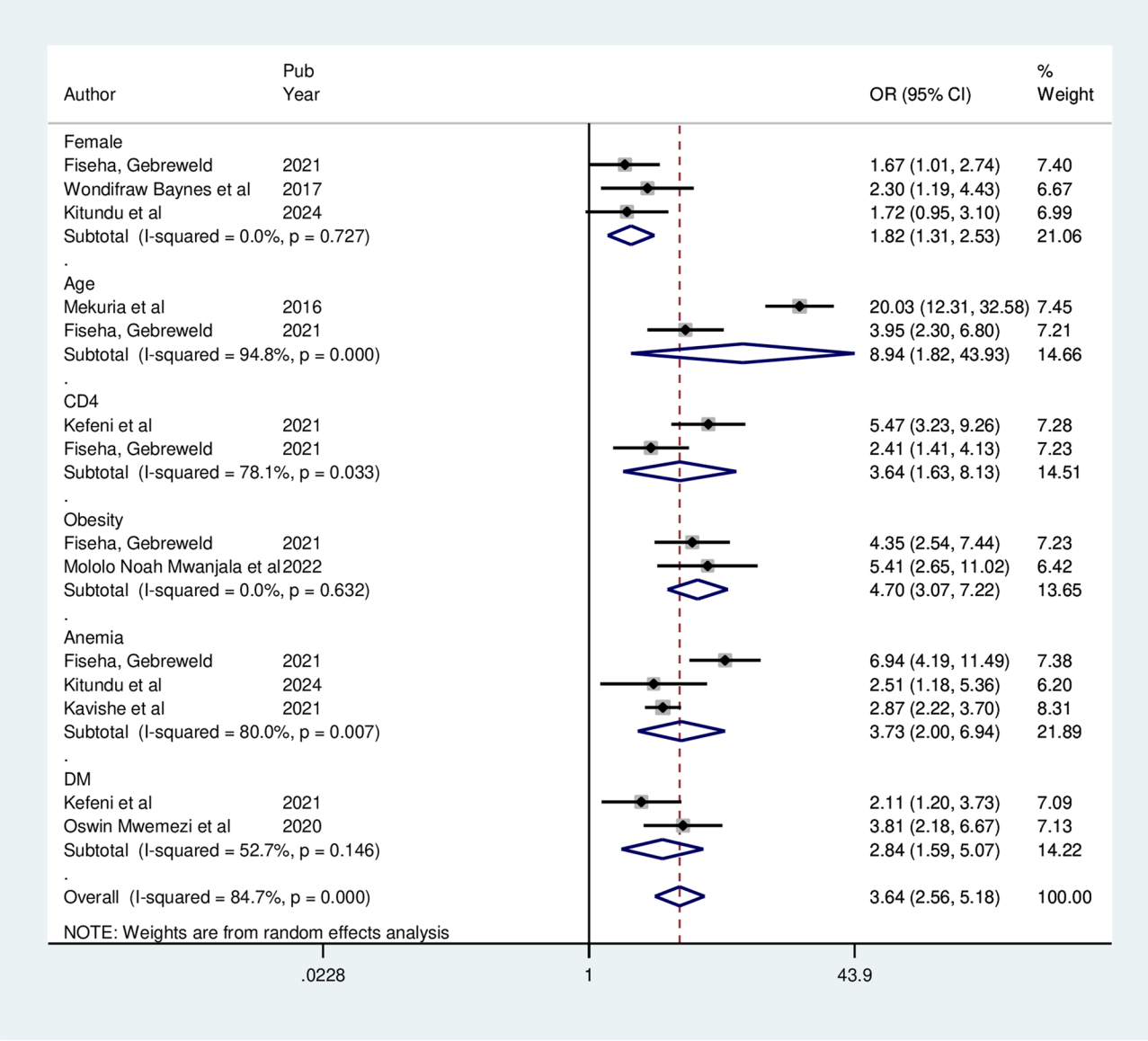

Fig. 8 Factors associated with kidney dysfunction among adults living with HIV

adipose tissue around the kidney and increased extracellular matrix within the kidney [63].

The study revealed that kidney dysfunction was more prevalent among female participants compared to males. Female sex was found to be an independent and significant factor for kidney dysfunction. These results are consistent with similar study conducted in U.S.A [64]. This trend may be attributed to the higher proportion of women living with HIV/AIDS in the included studies.

The findings also suggest that diabetes is a risk factor for kidney dysfunction. This result aligns with findings from similar study conducted in USA [64]. This could be attributed to diabetic nephropathy, a common complication of diabetes that decreases the glomerular filtration rate. Diabetes can harm the clusters of blood vessels in the kidneys responsible for waste filtration. Persistent blood glucose elevation levels affect the kidney's microvasculature, leading to nephrosclerosis [65].

This study indicates that patients with a low CD4 count are more prone to experiencing kidney dysfunction. When immunological AIDS is present (with a CD4 count below 200 cells/μL), it is commonly associated to the onset of opportunistic infections, cancers, and various vital organ disorders, all of which can impair kidney function. Furthermore, adults living with HIV who had anemia were more likely to develop kidney dysfunction compared with adults without anemia, This agreed with the report of a study in which low hemoglobin was found to be a predictor of renal dysfunction [66]. Kidney disease often leads to anemia because of lower

erythropoietin levels. Notably, the connection between hemoglobin levels and estimated glomerular filtration rate varied depending on HIV status [67]. Anemia associated inflammation contributes to the decline in GFR, anemia secondary to hypoxia, causing inflammation and fibrosis and loss of capillaries [68].

Limitations

As a strong point, the authors used some of the important major databases to search for original articles. However, this systematic review and meta-analysis is not free from limitations. Firstly, it solely considered articles published in English, potentially excluded relevant studies in other languages which could provide unique insights into kidney dysfunction among PLWHIV. The studies analyzed used different methods (CKD-EPI, MDRD, and Cockcroft-Gault) due to the absence of standardized methods for defining kidney dysfunction, which can lead to inconsistencies in prevalence estimation. In addition, although data were collected from multiple African countries, only a subset of regions are represented which limits the generalizability of the findings to the entire continent. Moreover, most studies included were cross-sectional, limiting the ability to assess causality or observe longitudinal trends. Substantial statistically significant heterogeneity was observed across studies which undermines the pooled estimate of kidney dysfunction suggests that chance could be responsible for between-study variability.

Conclusion and recommendations

This study revealed that the pooled prevalence of kidney dysfunction among adults living with HIV in Africa remains significant. Female sex, age ≥ 50 years, body mass index ≥ 30 kg/m², diabetes mellitus, CD4 count < 200 cells/mm³ and anemia were factors associated with kidney dysfunction. To reduce the morbidity and mortality associated with kidney dysfunction, it is advisable to create awareness and initiating early interventions through health education during their follow-up time, and initiating suitable medication at an early stage. In addition, our finding highlight the need for assessment of kidney function at baseline and regular monitoring of kidney function. Lifestyle changes to manage obesity, along with regular screening of kidney function, should be prioritized to reduce the risk of kidney dysfunction.

Abbreviations

GFR	Glomerular Filtration Rate
HIVAN	HIV-associated nephropathy
HIV	Human immunodeficiency Virus
PROSPERO	Prospective Register of Systematic Reviews
POR	Pooled Odds Ratio
STATA	South Texas Art Therapy Association

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Author contributions

WCT: hypothesized and designed the review, writing the proposal, data extraction, performed data analysis, and drafted the manuscript, quality appraisal, and interpretation of the findings. AMZ, GMA, and YAF: helped in data extraction and quality appraisal. Finally, all authors reviewed and approved the final manuscript.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Medical Nursing, Teda Health Science College, Gondar, Ethiopia
[2]Department of Clinical Midwifery, Teda Health Science College, Gondar, Ethiopia
[3]Department of Reproductive Health, Teda Health Science College, Gondar, Ethiopia
[4]Health Research Development Directorate, Amhara Public Health Institute, Bahir Dar, Ethiopia

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