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Authors

Banerjee, Tanushree
Frongillo, Edward A
Turan, Janet M
et al.

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Association of higher intake of plant-based foods and protein with slower kidney function decline in women with HIV

Tanushree Banerjee, PhD[1], **Edward A. Frongillo**[2], **Janet M. Turan**[3], **Lila A. Sheira**[4], **Adebola Adedimeji**[5], **Tracey Wilson**[6], **Daniel Merenstein**[7], **Mardge Cohen**[8], **Adaora A. Adimora**[9], **Igho Ofotokun**[10], **Lisa Metsch**[11], **Gypsyamber D'Souza**[12], **Margaret A. Fischl**[13], **Molly Fisher**[14], **Phyllis C. Tien**[15], **Sheri D. Weiser**[15]

[1]Division of General Internal Medicine, Department of Medicine, University of California, San Francisco CA

[2]Department of Health Promotion, Education, and Behavior, University of South Carolina

[3]School of Public Health, University of Alabama at Birmingham

[4]School of Nursing, University of California, San Francisco

[5]Department of Epidemiology & Population Health, Albert Einstein College of Medicine

[6]School of Public Health, SUNY Downstate Health Sciences University

[7]Department of Medicine, Georgetown University

[8]Chicago Women's Interagency HIV Study

[9]School of Public Health, University of North Carolina at Chapel Hill

[10]School of Medicine, Emory University

[11]School of Public Health, Columbia University

[12]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health

[13]Department of Medicine, University of Miami Health System

[14]Department of Medicine, Albert Einstein College of Medicine

[15]School of Medicine, University of California, San Francisco

Abstract

Background: We investigated whether lower dietary acid load in women living with HIV (WLWH) receiving antiretroviral therapy (ART) is associated with lower kidney function decline.

Correspondence: Tanushree Banerjee, PhD, Priscilla Chan and Mark Zuckerberg San Francisco General Hospital, 1001 Potrero Avenue, Bldg 10, Ward 13, 1311N, San Francisco, CA 94110., Tel: 628-206-6007, Fax: 628-206-5586, tanushree.banerjee@ucsf.edu.

Statement of authors' contributions to manuscript

The authors' responsibilities were as follows—TB, SDW: designed the research; LAS: data curation; TB: analyzed data or performed the statistical analysis; TB, SDW: wrote the paper, had primary responsibility for the final content, and obtained data from the Women's Interagency HIV Study (WIHS) database; and all authors: read and approved the final manuscript.

Disclosures: TB, EAF, JMT, LAS, AA, TW, DM, MC, AAA, IO, LM, GS, MAF, MF, PCT, and SDW, no conflicts of interest.

Setting: 1,608 WLWH receiving ART in WIHS cohort with available diet data and a baseline estimated glomerular filtration rate (eGFR)≥15 ml/min/1.73 m^2.

Methods: A brief dietary instrument conducted from 2013–2016 under the Food Insecurity Sub-Study was used for assessing fruits and vegetables (FV) and protein intake. A mixed effects model with random-intercept and slope was used to estimate subjects' annual decline rate in eGFR and the association between FV intake, adjusting for socio-demographics, serum albumin, comorbidities, time on ART, ART drugs, HIV markers, and baseline eGFR. We evaluated whether markers of inflammation mediated the effect of FV intake on decline in eGFR, using causal mediation analysis.

Results: We found a dose-response relationship for the association of FV intake and eGFR decline, with lesser annual decline in eGFR in the middle and highest tertiles of FV intake. An increase of 5 servings of FV intake per day was associated with a lower annual eGFR decline (−1.18 [−1.43, −0.94]). On average, 39% of the association between higher FV intake and slower eGFR decline was explained by decreased levels of inflammation.

Conclusion: Plant-rich diets was associated with slower decline in kidney function. Inflammation is a potential path through which diet may affect kidney function. The findings support an emerging body of literature on the potential benefits of plant-rich diets for prevention of chronic kidney disease.

Keywords

dietary intake; fruits and vegetables; kidney function; inflammation; HIV

Introduction

Antiretroviral therapy (ART) has resulted in a marked decrease in AIDS-related conditions and improved survival among people with HIV (PWH).[1] However, with increased longevity, non-AIDS related comorbidities such as chronic kidney disease (CKD) have become increasingly important causes of morbidity and mortality in this population. PWH receiving ART are at disproportionately increased risk of CKD due to development of comorbidities associated with aging such as diabetes and hypertension as well as potential for nephrotoxicity from prolonged ART exposure.

The kidneys play a central role in the regulation of body fluids, electrolytes, and acid-base balance. Diets in industrialized societies are shifting from relatively alkali-predominant toward more acid-predominant diets because they are deficient in fruits and vegetables, and high in sulfur-rich proteins and phosphorus.[2] This dietary shift may play a role in the regulation of chronic inflammation. The consumption of more fruits and vegetables typically lowers the dietary acid content while meat, eggs, cheese, grain products, sugar, and rice are relatively strong net acidifying foods.[2–6] Nutrition has been known to strongly influence acid-base balance, and imbalances in endogenous acid-base equilibrium due to diet may lead to inflammation.[7,8] Consumption of a diet abundant in acid precursors over time results in multiple derangements including lower buffering capacity, and as CKD progresses, a decreased ability of the kidneys to excrete the excess acid.[9] Such diets are believed to have a proinflammatory effect and can induce metabolic acidosis in individuals with reduced

glomerular filtration rate (GFR), including otherwise healthy older persons.[10,11] On the other hand, diets high in base precursors such as fiber may have an anti-inflammatory effect and have been shown to ameliorate metabolic acidosis.[12]

Dietary acid load is a measure of balance between acid-inducing foods and base-inducing foods.[2,13] Changing from standard industrialized society diets to a low-phosphorous vegan diet has shown to improve metabolic acidosis in patients with advanced CKD.[14] Moreover, added fruits and vegetables has reduced urine net acid excretion, consistent with reduced net endogenous acid production[10], in individuals with CKD stage 2 (estimated GFR, 60–89 ml/min per 1.73 m2) but without metabolic acidosis.[15] Further, our research along with other epidemiological and small clinical studies have previously shown a direct association between high dietary acid load due to higher consumption of animal protein and lower potassium enriched fruits and vegetables and CKD progression.[16–18] Together, these studies suggest that added fruits and vegetables can reduce the acid load, improve metabolic acidosis in CKD and slow progression to end-stage kidney disease. To the best of our knowledge, it is unknown if lowering the acid load in the diet among women living with HIV (WLWH) on antiretroviral therapy (ART) slows kidney function decline and if reduced inflammation may be on the causal path of this association.

In this study, we examined the association of fruits and vegetables intake (marker of low dietary acid load) and protein intake (marker of high dietary acid load) with decline in kidney function, among WLWH receiving ART. We hypothesized that a low dietary acid load in PLW receiving ART for a long duration slows decline in kidney function and that reduced inflammation mediates this association.

Materials and Methods

Participants Characteristics and Procedures

Data were collected from WLWH participating in the Women's Interagency HIV Study (WIHS).[19,20] WIHS is a multi-site prospective study investigating HIV disease progression, comorbidities, and the behavioral impact of HIV among women in the US, now part of the MACS-WIHS Combined Cohort Study (MWCCS, https://statepi.jhsph.edu/mwccs/). Established in 1994, data were collected from participants in six US sites (Bronx, Brooklyn, Washington DC, Chicago, Los Angeles, and San Francisco) every 6 months via interviews, physical assessments, and laboratory tests. To further enhance the representativeness of the cohort, new participants were enrolled between 2013–2015 at sites in the US South; including Atlanta, Birmingham, Jackson, Miami, and Chapel Hill.[20] The median age of WIHS WLWH is 50 years. Around 75% of WIHS WLWH identify as African American, 14% as White, and 14% as Hispanic. All participants provided written informed consent, with study activities being approved by each site's Institutional Review Board.

This secondary data analysis used retrospective data collected under the food insecurity sub-study (grant # R01MH095683) from 2013 to 2016 biannually from nine sites across the United States participating in the WIHS. To fit within the data collection procedures of WIHS and limit respondent burden, we used a brief dietary instrument to assess dietary behavior rather than a method intended to estimate quantitatively the amounts of nutrients.

For this study, we restricted analyses to WLWH on ART at the time of the first available dietary instrument and who continued with ART till the end of the follow up period (n=1,624). We further excluded women with an eGFR at baseline of less than 15 ml/min/1.73 m2 (due to the lack of information on participant's dialysis history) or who did not have available dietary data and data on markers of inflammation for analysis resulting in a sample size of 1,608 (Supplemental Figure 1).

Primary exposure variables

Dietary intake was measured using an adapted version of the Year 2000 National Health Interview Survey multifactor brief dietary instrument.[21] For many studies, including studies in the WIHS, the brief dietary instrument has been found to successfully provide information about differences and changes in dietary behavior. The diet quality instrument was conducted among all WIHS women from 2013 to 2016 annually under the Food Insecurity Sub-Study. This dietary instrument assessed the dietary intake frequencies as times per day, week, month, or year of 18 food line items, representing 50 foods or food groups. All intake frequencies were converted to daily intake frequencies. Missing values (<1%) were imputed under the assumption of missing at random to ensure complete cases. The dietary instrument was used for assessing fruits and vegetable intake and protein intake (Supplementary Table 1).

Outcomes

The primary outcome was eGFR slope in each rolling window, expressed in mL/min/1.73 m2 per year, that is the annual change in eGFR in each of the three time periods ranging from each participant's first visit to end of 12 months, 13 months to 24 months, and finally 25 months to end of 36 months. We calculated eGFR using the 2009 CKD Epidemiology Collaboration creatinine equation.[22] Serum creatinine was measured semi-annually at the clinical labs of each WIHS site using the modified Jaffe method, traceable to isotope dilution mass spectrometry.

Covariates

We selected clinical and sociodemographic covariates based on previous literature and theory.[16,23,24] The socio-demographic covariates were age at enrollment, race/ethnicity, self-reported educational attainment categorized as < high school, ≥high school, race/ethnicity, and annual household income (≤$36,000 [ref] vs. >$36,000). Clinical covariates were body weight (kg), body height (m), serum albumin, hypertension, diabetes status, and smoking. Hypertension status was a composite variable defined as systolic blood pressure>=140 or diastolic blood pressure>=90, self-report, or use of anti-hypertensive medicines at visit. Diabetes status was defined as if ever self-reported anti-diabetic medication or fasting glucose>=126 mg/dL or HbA1C>=6.5% or self-report. HIV-related clinical covariates included current (i.e., at index visit) CD4+ count (cells per μL), current CD8+ count (cells per μL), current HIV-1 RNA (copies/mL), and years on ART. We also evaluated current ART drug regimen that included tenofovir dixoproxil fumarate, or other drugs influencing creatinine such as dolutegravir, rilpivirine and cobicistat. Across all covariates, <1% of the data were missing.

Inflammatory Markers

We used serum markers of monocyte activation (soluble (s) CD14, sCD163) and systemic inflammation (IL-6, TNF-R1). To increase the power for testing associations, we created a summary index for individual inflammatory markers by rescaling each individual biomarker to have a mean of zero and a standard deviation (SD) of 1 so that normalized z-scores were obtained for each biomarker.[25] The z-scores for serum measures of inflammation were averaged to create the inflammation status variable.

Statistical Analysis

The outcome measure for this study was the annual rate of eGFR decline. Characteristics at study participants' first visit were examined according to tertiles of fruits and vegetables intake using $\chi 2$ tests for categorical variables and ANOVA for numeric variables. Our first analysis examined the association between fruits and vegetables intake and inflammation in our study population using a mixed-effects model adjusted for all covariates. We used a mixed effects model with random intercepts and slopes to estimate the subjects' annual decline in eGFR. We used a mixed effects model with age as the time scale to examine the independent predictive value of fruits and vegetables intake and (ii) protein intake (categorically as tertile intake with the lowest tertile as the reference category) for decline of eGFR, adjusting for potential covariates and baseline eGFR. We further examined the intake of fruits and vegetables as a continuous variable (considering an increase of 5 servings for all participants) with decline of eGFR. We used age as the time scale since that allows the model to compute risk estimates for individuals with the same age irrespective of the years of follow up.[26,27] Since age is a risk factor for CKD as well as its progression, we would expect the risk to change more as a function of age than as a function of "time on study". Covariates for adjustment were chosen if they were associated with progression of CKD in univariate analyses ($P<0.10$).

Mediation Analysis:

We tested the mediation effect of inflammation by examining the indirect effects in mediation analysis by using a method described by Bauer et al.[28] The outcome model has random intercepts and random slopes for the exposure, the mediator, and their interaction. In this analysis, we calculated the indirect effect and test the importance of the indirect path– that lower intake of fruits and vegetables affects decline in GFR through the increased levels of inflammation. The mediator was lagged relative to the exposure, and hence data on inflammation were used from 2014 and 2015 only.

Results

Descriptive Statistics

There was a wide range in serum creatinine among women with HIV ranging from 0.48 to 8.69 mg/dl with a mean ± SD of 1.20 ± 0.85 mg/dl. Participant demographics are summarized in Table 1 and Supplementary Table 2. Our population was comprised mainly of women with the mean age of 47.6 years and blacks (68.2%). One-third (33.2%) of the

women did not complete high school while 86.3% had an annual household income of less than $36,000. Hypertension (49.4%) was common in this cohort.

Figure 1 shows that the intake of fruits and vegetables was relatively low, and the median servings per day was 1.28 (25^{th}–75^{th} percentile: 0.8–2.0). The median intake of protein was 3.1 servings/day (25^{th}–75^{th} percentile: 2.1 to 4.4 servings/day) (Figure 2).

Association of fruits and vegetables intake and protein intake with decline in kidney function using mixed-effects model

Unadjusted analysis demonstrated that moderate and high FV intake was associated with a slower annual eGFR decline (over a median 2 year of follow-up, Table 2). Adjustment for age and race attenuated the decline in eGFR to −1.09 (−2.03, −0.13) in the highest tertile of intake and to −0.32 (−0.84, 0.19) in the middle tertile. On adjustment for all covariates, and baseline eGFR, the association between the middle and higher tertile of fruits and vegetables intake and decline in eGFR was lessened. A dose-response relationship was noted in the fully adjusted model (β [95% CI]: −0.60 (−1.14, −0.06) in the middle tertile and −1.27 (−2.04, −0.45) in the highest tertile; ptrend=0.001).

On testing the association between the increase in servings of fruits and vegetables per day (continuously per increase in 5 servings/day) in all participants and annual decline in eGFR, we noted the estimated decrease in the decline in eGFR as −1.18 (−1.43, −0.94).

On examining the association of protein intake and decline in eGFR, the highest tertile of protein intake was associated with a lower decline in eGFR (−0.85 [−1.49, −0.14] when adjusted for the potential confounders, Table 3).

Association between FV intake and inflammation and kidney function

Unadjusted analysis showed that higher intake of FV was associated with lower levels of inflammation (as measured by the summary index for inflammatory markers, β [95% CI]: −0.17 [−0.29, −0.03]). After adjustment for potential confounders, higher intake of FV remained associated with lower levels of inflammation (−0.22 [−0.35, −0.06]). Furthermore, increased levels of inflammation markers were associated with a greater decline in eGFR (3.55 (2.85–4.35]). The association remained upon adjustment for cofounders (2.05 [1.60–2.58]).

Association of higher intake of fruits and vegetables and slower decline in kidney function mediated by decreased levels of inflammation

We determined the estimated average indirect effect of higher intake of fruits and vegetables on slower decline in kidney function to be −0.45 (95% CI= −0.72, −0.12) and the estimated average total effect of higher intake of fruits and vegetable on slower decline in kidney function to be −1.17 (95% CI= −1.48, −0.82), Figure 3. The effect estimates indicate that higher intake of fruits and vegetables reduce inflammation and, on average, about 39% of the total effect of higher intake of fruits and vegetables (decreased diet acid load) on slower decline in eGFR was indirect and mediated by the lower state of inflammation. Mediation for each marker of inflammation considered separately was consistent with the mediation by

the summary index of inflammation, with the percent mediated being 26.1, 18.2, 8.6, and 16.5 for CD14, sCD163, IL-6, and TNF-R1, respectively (Supplementary Table 3).

Discussion

The present study examined the association between intake of FV and risk of eGFR decline among women receiving ART among a large geographically diverse cohort of women with HIV in the United States. We found that repeated higher intake of FVs was associated with a slower rate of decline in eGFR, suggesting lower dietary acid load diet due to a daily higher intake of FVs may be associated with slowing decline in kidney function.

Diet composition is known to influence acid–base balance by providing acid or base precursors. Depending on the quantity of the acid load and kidney function, diets high in acid load can induce an acid-retaining state, which may be associated with the development of metabolic alterations such as hypertension, progression of CKD, and other complications.[16,29,30] To our knowledge, no prior study has investigated the association between a lower diet dependent acid load and kidney function in people living with HIV. Findings from the current study corroborate findings from prior studies that have shown progressive GFR decline by acid-inducing diets in subjects with relatively mild CKD (eGFR=60–89 ml/min per 1.73 m^2. The predominant anions in FVs are citrate and malate, and when metabolized, they release bicarbonate and thus contribute alkali to the body exhibiting beneficial metabolic effects. Furthermore, FVs that are high in fiber promote the growth of saccharolytic bacteria[31], which produce short chain fatty acids (alkali) and other anti-inflammatory compounds, and lower the generation of uremic toxins.[32] Uremic toxins, such as P-cresol or indoxyl sulfate, are involved in the onset and progression of CKD through promotion of fibrosis in the kidney.[33] Antioxidants in FVs may neutralize reactive oxygen species, which play a role in CKD progression, and reduce DNA damage[34], and glucosinolates in cruciferous vegetables induce detoxifying enzymes.[35] High FV intake may also indirectly reduce risk of CKD progression by displacement of unhealthy foods high in saturated fat, trans fat, glycemic load and sodium.

Lower financial means and living in certain communities may affect the ability of individuals to obtain a diet rich in fruits and vegetables. Studies of the food and low socio-economic status environment suggest that low-income individuals often live in neighborhoods where there are few full-service grocery stores and may not have easy access to transportation to allow for shopping at such stores in outlying areas. Limited access to nutritious food and relatively easier access to less nutritious food may be linked to poor diets and, ultimately, to diet-related diseases. Given this, effects on eGFR reduction due to FV would have greatly diminished when adjusted for income and education. However, the association remained significant.

We found that higher protein intake was associated with a slower decline in kidney function. Though prior studies suggest that high protein intake may promote kidney damage by chronically increasing glomerular pressure and hyperfiltration[36–38], growing evidence show that the more important determinant of the effect of dietary protein on CKD progression is the quality of the ingested protein (i.e., whether it induces acid-production [like most animal

protein] or base production [like most fruit and vegetable protein]) when ingested rather than the quantity of protein ingested.[3,39–42] This study did not evaluate the association between the quality of the ingested protein and decline in kidney function which may explain this unexpected finding.

The mediating role of circulating biomarkers of serum macrophage inflammation and systemic inflammation in the association between the lower intake of fruits and vegetables and decline in kidney function suggests that inflammation might be one of the paths through which diet can affect kidney function. Serum levels of CD14 and CD163 in HIV-infected participants helps identify individuals with ongoing inflammation despite successful ART.[43] Increased generation of IL-6 and TNF-R1 is noted in metabolic alterations such as CKD and is largely caused by chronic inflammation and oxidative stress. The kidneys play a central role in maintaining homeostasis in the body and can be the target of inflammatory disorders caused by the immune system's response to the presence of HIV.[44] Healthier diets (e.g., rich in fruits and vegetables such as the Mediterranean diet) typically have been associated with lower inflammation levels, whereas Western-style diets (e.g., high in fat and simple carbohydrates) have been associated with higher levels of inflammatory markers.[45–48] In our study, we found a higher intake of FV to be associated with lower levels of the markers of systemic inflammation in women living with HIV.

Several limitations of our study should be considered. First, dietary assessment was limited to 18 self-reported food line items, and only intake frequency was queried; referent serving sizes were not provided; details of the foods comprising each line item are unknown; and nutrient content is not available. We used a dietary screener that was validated and developed by the National Cancer Institute[21] for use in similar communities. Despite the lack of information about total dietary and energy intakes, there is precedent for using key indicator foods to examine diet quality.[49,50] Second, our findings cannot be generalized to men or younger women. Lastly, we did not have the necessary dietary components to estimate diet-dependent acid load and have used intake of fruits and vegetables and protein as a marker for dietary acid load.

These limitations are counterbalanced by several strengths of this study. This is the first longitudinal study examining decline in kidney function in association with lowering of diet-dependent acid load intake (higher intake of fruits and vegetables and lower intake of protein) in HIV-positive women. Prior studies by Banerjee et al.[52,53] have documented the impact of food insecurity and unhealthy diets on clinical conditions of CKD and its progression using the National Health and Nutrition Examination Survey linked to US Renal Data System Registry.

The findings from this study show an association between higher intake of fruits and vegetables and slower decline in kidney function, supporting an emerging body of literature on the potential benefits of plant-rich diets for primary CKD prevention. This result suggests inflammation is a potential path through which diet may affect kidney function. This is the first study in a population living with HIV that has examined the association of diet dependent acid load characterized by higher intake of fruits and vegetables with kidney function, a population in whom comorbid kidney diseases become increasingly common

with age. Our results suggest that the alkali-based diet in people with HIV receiving antiretroviral therapy slows decline of kidney function despite potential nephrotoxic effects of ART. Findings from our study, if confirmed in clinical trials, may have application for both population-wide and high-risk approaches to CKD prevention and management in various settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Sharing

Data described in the manuscript, code book, and analytic code will be made available upon request pending [e.g., application and approval, payment, other].

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Research in Context

Evidence before this study

Although small clinical studies and cohort studies in chronic kidney disease patients have shown that diets rich in fruits and vegetables can slow the progression of kidney damage, a search of PubMed conducted before commencement of this study using the terms “kidney disease progression” AND “HIV” AND “fruits and vegetables” for studies published in English between Jan 1, 2005, and July 31, 2019, yielded no results suggesting that no prior study in HIV population had examined if lowering the acid load in the diet among subjects on antiretroviral therapy slows kidney function decline. Over the past four decades, advances in HIV treatment have contributed to a longer life expectancy for people living with HIV. However, with prolonged survival, recipients of ART face adverse consequences beyond HIV itself, including diseases associated with aging such as diabetes, hypertension, and chronic kidney disease. Apart from beneficial impact of early ART initiation on HIV associated nephropathy, studies exploring other treatment strategies for slowing kidney disease progression have not been conducted rigorously.

Added value of this study

We analyzed data from the Women’s Interagency HIV study (WIHS, now part of the MWCCS) in women living with HIV receiving ART. We used a mixed effects model with age as the time scale to examine the independent predictive value of fruits and vegetables (FV) intake for decline of eGFR. The primary finding shows a dose-response relationship for the association of FV intake and eGFR decline suggesting plant-based diets may be effective in slowing decline in kidney function. Causal mediation analysis showed that 39% of the association between higher FV intake and slower eGFR decline was explained by decreased levels of inflammation. This is the first study in a population living with HIV that has examined the association of diet dependent acid load with kidney function, a population in whom comorbid kidney diseases become increasingly common with age.

Implications of all the available evidence

The potentially deleterious effect of a diet low in plant-based foods on kidney health mediated through increased levels of inflammatory markers, supported by our findings and those of other investigators in chronic kidney disease, suggests the potential utility of the modulation of inflammatory properties of diet, in strategies to prevent kidney disease. If confirmed in clinical trial, this knowledge may have application for both population-wide and high-risk approach to CKD prevention and control in various settings.

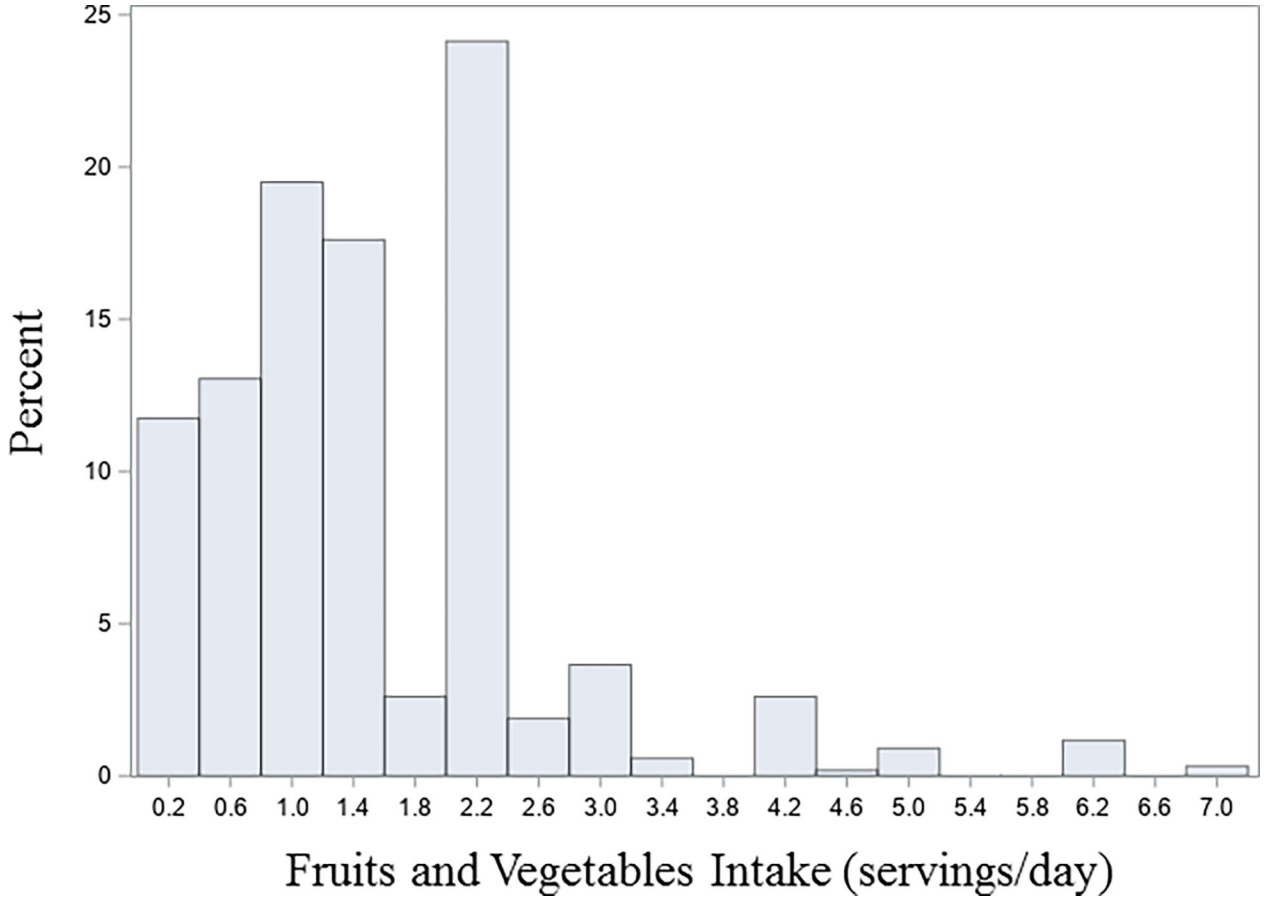

Figure 1:
Frequency distribution of intake of fruits and vegetables per day in 1,608 women living with HIV

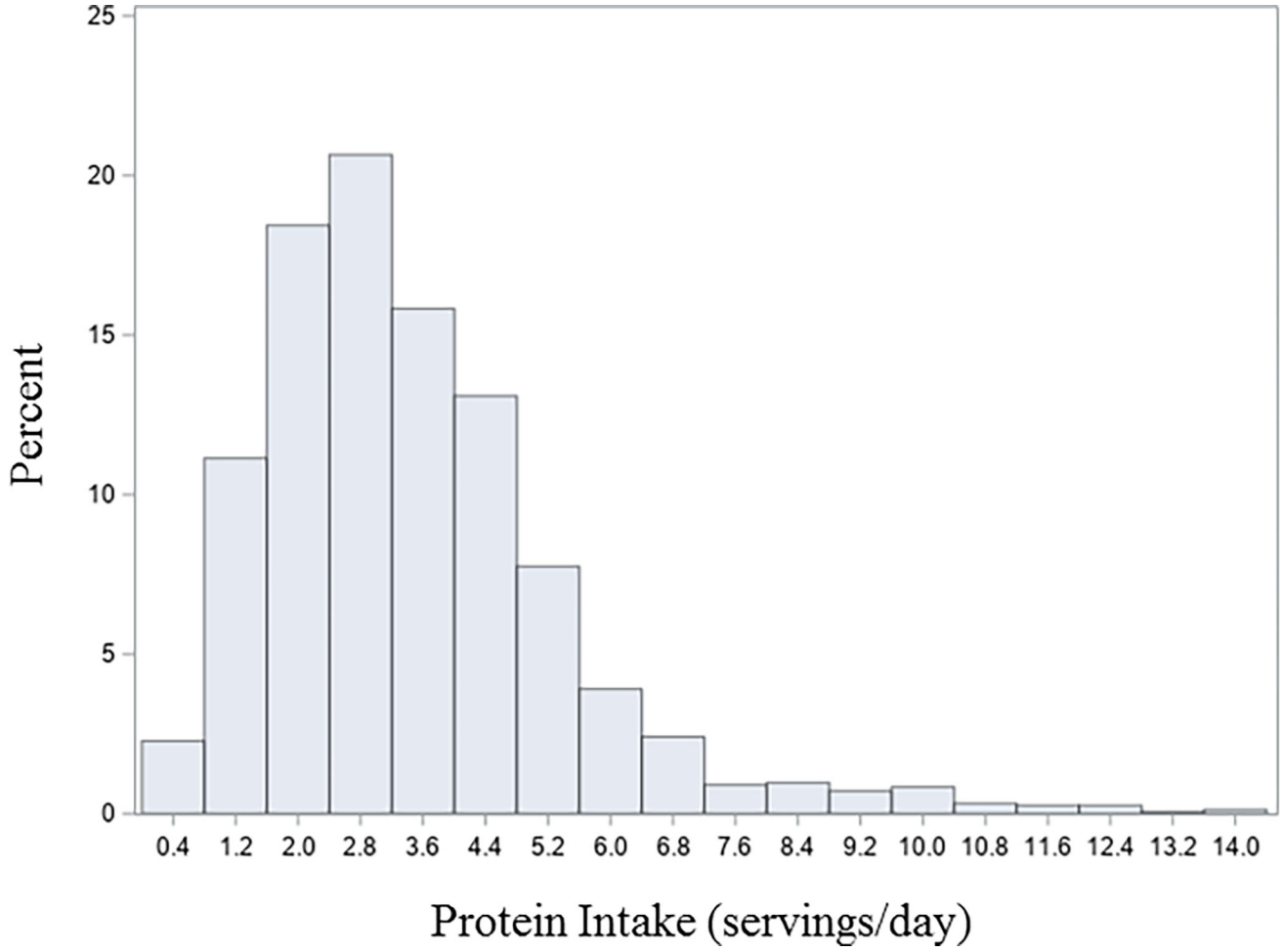

Figure 2:
Frequency distribution of intake of protein per day in 1,608 women living with HIV HIV-positive women

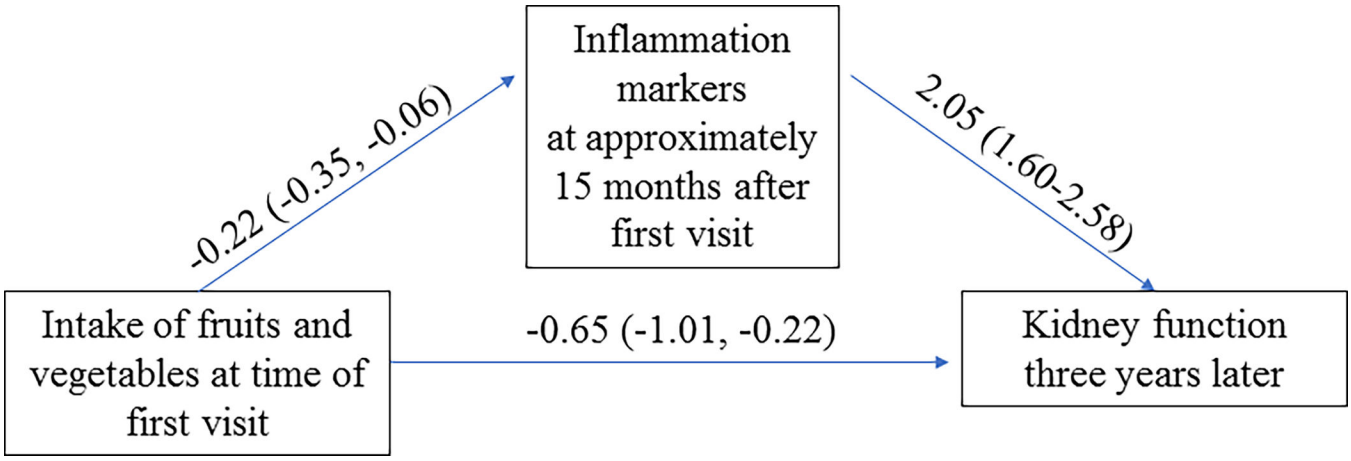

Figure 3:

Decreased levels of inflammation markers at months after first visit mediate the effect of higher intake of fruits and vegetables at time of first visit on improvement in kidney functional markers three years later in 1,608 women living with HIV

Note. Associations are presented as path coefficients (adjusted), see results section.

Table 1:

Baseline Characteristics of women living with HIV by tertiles of fruits and vegetables intake (N=1,608)

	Total	Lowest Tertile (0–1.2 servings/day, n=413))	Middle Tertile (1.2–2.3 servings/day, n=626)	Highest Tertile (≥2.3 servings/day, n=569)	Linear Trend Test
Age (in yrs), mean±SE	47.6±0.2	47.7±0.4	47.6±0.3	46.7±0.6	0.18
Race					0.08
White, non-Hispanic	193 (12)	32 (7.7)	94 (15)	67 (11.8)	
Black, non-Hispanic	1096 (68.2)	306 (74.1)	405 (64.7)	385 (67.7)	
Hispanic	241 (15)	54 (13.1)	103 (16.5)	84 (14.8)	
Other	78 (4.8)	21 (5.1)	24 (3.8)	33 (5.7)	
Education Level (<high school), %	33.2	35.6	33.4	24.2	0.004
Annual Household Income (<36,000), %	86.3	88.5	86.3	79.4	0.02
Body Mass Index (kg/m2), mean ±SE	31.0±0.2	31.1±0.4	31.1±0.3	30.8±0.7	0.76
Diabetes Status (yes), %	19.1	34.2	53.9	11.9	0.18
Hypertension Status (yes), %	49.4	39.3	50.6	10.1	0.03
Smoking Status (yes), %	38.6	38.7	53.2	8.1	0.02
Serum Albumin (gm/dL), mean±SE	4.1±0.02	4.1±0.03	4.1±0.02	4.2±0.03	0.05
eGFR (ml/min/1.73 m2), mean±SE	94.1±0.6	93.1±1.0	94.2±0.8	98.2±1.8	0.041
Antiretroviral Drugs, %					0.04
Tenofovir Dixoproxil Fumarate	43.7	52.3	37.3	10.4	
TDF/Emtricitabine	28.5	55.8	35.7	8.4	
Dolutegravir	25.8	57.4	34.8	7.8	
Rilpivirine	0.3	56.1	35.6	8.3	
Cobicistat	1.7	58.3	25.0	16.7	
CD4 cell count, cells/μL, mean±SE	592.6±7.5	580.8±13.0	583.2±22.4	600.6±10.1	0.02
CD8 cell count, cells/μL, mean±SE	783.9±9.7	791.0±16.9	784.6±13.2	756.4±25.4	0.03
Viral Load, copies/ml, median (Q1–Q3)	38.0 [20.0–173.5]	42.6 [22.5–140.0]	38.1 [21.2–172.0]	35.6 [20.0–140.0]	0.035

P value for trend for continuous dependent variables were calculated with the use of linear regression.

Table 2:

Association between the intake of fruits and vegetables (in tertiles and for an increase of 5 servings per day) and eGFR decline in women living with HIV

	Fruits and Vegetables Intake, β (95% CI)			
	Lowest Tertile (0–1.2 servings/day)	**Middle Tertile (1.2–2.3 servings/day)**	**Highest Tertile (≥2.3 servings/day)**	**Continuous (increase of 5 servings/day)**
Unadjusted	β=0 (Reference)	−0.35 (−0.86, −0.16)	−1.06 (−2.01, −0.16)	−1.42 (−1.80, −1.06)
Model 1	β=0 (Reference)	−0.32 (−0.84, 0.19)	−1.09 (−2.03, −0.13)	−1.36 (−1.68, −1.04)
Model 2	β=0 (Reference)	−0.27 (−0.80, 0.26)	−1.02 (−1.94, 0.10)	−1.30 (−1.63, −0.97)
Model 3	β=0 (Reference)	−0.30 (−0.82, 0.25)	−1.00 (−1.95, 0.12)	−1.35 (−1.67, −0.98)
Model 4	β=0 (Reference)	−0.65 (−1.04, 0.02)	−1.37 (−2.23, −0.42)	−1.24 (−1.55, −0.94)
Model 5	β=0 (Reference)	−0.61 (−1.13, −0.08)	−1.32 (−2.17, −0.48)	−1.20 (−1.46, −0.91)
Model 6	β=0 (Reference)	−0.60 (−1.14, −0.06)	−1.27 (−2.04, −0.45)	−1.18 (−1.43, −0.94)

Model 1: Unadjusted+ age+ race; Model 2: Model 1+ education+ household income; Model 3: Model 2+ serum albumin+ hypertension+ diabetes+ smoking; Model 4: Model 3+ time on antiretroviral drugs+ ART drugs; Model 5: Model 4+CD4 count+CD8 count+ log viral load; Model 6: Model 5+ baseline kidney function

Table 3:

Association between the intake of protein (in tertiles) and eGFR decline in women living with HIV

	Protein Intake, β (95% CI)		
	Lowest Tertile (0–2.3 servings/day)	**Middle Tertile (2.3–3.7 servings/day)**	**Highest Tertile (≥3.7 servings/day)**
Unadjusted	β=0 (Reference)	0.08 (−0.54, 0.71)	−0.41 (−1.06, 0.23)
Model 1	β=0 (Reference)	0.07 (−0.56, 0.69)	−0.45 (−1.10, 0.18)
Model 2	β=0 (Reference)	0.10 (−0.53, 0.74)	−0.43 (−1.09, 0.23)
Model 3	β=0 (Reference)	0.13 (−0.49, 0.75)	−0.47 (−1.13, 0.19)
Model 4	β=0 (Reference)	−0.07 (−0.69, 0.57)	−0.70 (−1.36, −0.03)
Model 5	β=0 (Reference)	−0.08 (−0.70, 0.54)	−0.82 (−1.50, −0.15)
Model 6	β=0 (Reference)	−0.10 (−0.71, 0.53)	−0.85 (−1.49, −0.14)

Model 1: Unadjusted+ age+ race; Model 2: Model 1+ education+ household income; Model 3: Model 2+ serum albumin+ hypertension+ diabetes+ smoking; Model 4: Model 3+ time on antiretroviral drugs+ ART drugs; Model 5: Model 4+CD4 count+CD8 count+ log viral load; Model 6: Model 5+ baseline kidney function