Estimated glomerular filtration rate in people living with HIV

Estimativa da taxa de filtração glomerular em pessoas vivendo com HIV

Estimación de la tasa de filtración glomerular en personas que viven con el VIH

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Abstract
Objective: To evaluate the factors associated with the estimated Glomerular Filtration Rate (eGFR) in people living with HIV.
Methods: Cross-sectional and analytical study evaluating 340 people in outpatient care in the city of Ribeirão Preto-SP. eGFR was calculated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. Univariate analysis was performed with Chi-square and Fisher's exact tests, with $p < 0.05$.
Results: It was identified that 114 (34.1%) of the participants presented changes in Glomerular Filtration, of which (90) 27.5% were classified in stage 2, 15 (4.5%) in stage 3A and 07 (2.1%) in stage 3B.
Conclusion: The study demonstrated that the variables gender, age, hypertension, diabetes, BMI and time of diagnosis were associated with Glomerular Filtration Rate. The importance of the complete follow-up of PLHIV is emphasized, as it can prevent renal dysfunction.

Resumo
Objetivo: Avaliar os fatores associados à estimativa da Taxa de Filtração Glomerular (eTFG) em pessoas vivendo com HIV.
Métodos: Estudo transversal e analítico, com avaliação de 340 pessoas em atendimento ambulatorial no município de Ribeirão Preto-SP. Calculou-se a eTFG através da fórmula *Chronic Kidney Disease Epidemiology Collaboration* (CKD-EPI). Foi realizado análise univariada com os testes Qui-quadrado e Exato de Fisher, com $p<0,05$.
Resultados: Identificou que 114 (34,1%) dos participantes apresentaram alterações na Filtração Glomerular, dos quais (90) 27,5% foram classificadas em estágio 2, 15 (4,5%) em estágio 3A e 07 (2,1%) em estágio 3B.
Conclusão: O estudo evidenciou que as variáveis sexo, idade, hipertensão, diabetes, IMC e tempo de diagnóstico apresentaram associação com a Taxa de Filtração Glomerular. Ressalta-se a importância do acompanhamento integral de PVHIV para a tomada de decisões de modo a prevenir a ocorrência de disfunções renais.

Resumen
Objetivo: evaluar los factores asociados a la estimación de la tasa de filtración glomerular (eTFG) en personas que viven con el VIH.
Métodos: estudio transversal y analítico, con evaluación de 340 personas que reciben atención ambulatoria en el municipio de Ribeirão Preto, São Paulo. Se calculó la eTFG a través de la fórmula *Chronic Kidney Disease Epidemiology Collaboration* (CKD-EPI). Se realizó un análisis univariado con la prueba ^{2} de Pearson y la prueba exacta de Fisher, con $p<0,05$.
Resultados: se identificó que 114 participantes (34,1%) presentaron alteraciones en la filtración glomerular, de los cuales 90 (27,5%) fueron clasificados como nivel 2, 15 (4,5%) como nivel 3A y 7 (2,1%) como nivel 3B.
Conclusión: el estudio demostró que las variables sexo, edad, hipertensión, diabetes, IMC y tiempo de diagnóstico presentaron relación con la tasa de filtración glomerular. Se destaca la importancia del seguimiento integral de PVV para la toma de decisiones a fin de prevenir el desarrollo de una insuficiencia renal.

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Introduction

The advent of antiretroviral therapy (ART) has resulted in multiple benefits for people living with HIV (PLHIV), such as improved quality of life, viral suppression and longevity, making AIDS a chronic disease.[1] However, ART associated with the chronic inflammation involved in the pathophysiology of HIV infection, also causes important metabolic, renal and cardiovascular changes in this population.[2,3]

According to the most recent reports of the Joint United Nations Program on HIV/Aids, as of June 2017, there were about 36.7 million people living with HIV worldwide. It is estimated that in Brazil, 490,000 people are being treated with antiretrovirals (ARVs).[4]

Over time, with the chronicity of HIV/AIDS infection, PLHIV have naturally become exposed to chronic-degenerative processes, which were not manifested before due to the early mortality associated with the disease. Chronic diseases such as Diabetes Mellitus (DM), Systemic Arterial Hypertension (SAH), Cardiovascular Diseases (CVD) and Chronic Kidney Disease (CKD) have become the focus of research in this population.[2,3,5]

Changes in renal structure and function are commonly found in PLHIV before initiation of ART; after cumulative exposure to antiretroviral (ARV) medications, these changes may be more frequent, especially involving nephrotoxic agents.[6] Several studies evaluating CKD in this population, showed that reduction in the estimated Glomerular Filtration Rate (eGFR) is the basis for the identification of CKD.[3,6,7]

CKD is a condition that has a strong impact on the quality of life of PLHIV and on the provision of health care. Thus, research that seeks to identify the relationship between this pathology and HIV, evaluating the real impact of this disease associated with HIV infection, can guide actions in health and a provide a better patient care.[8]

Considering that changes in the Glomerular Filtration Rate may occur due to the HIV infection and/or the use of ART, the objective of this study was to evaluate the factors associated with the estimated Glomerular Filtration Rate in people living with HIV.

Method

This is a cross-sectional, analytical study carried out in the five Specialized Care Services (SCS) for people living with HIV in the city of São Paulo, from October 2014 to December 2016.

The non-probability consecutive sampling was stratified by unit of care and based on the number of patients taking antiretroviral therapy. The study included individuals over 18 years old, known to be HIV-positive, on ART for at least 6 months, of both genders and who were on outpatient clinical follow-up at the service.

Pregnant women and individuals in confinement, such as prisoners, institutionalized patients or patients in supported housing were excluded from the study.

Data were collected through individual interviews and medical records. The interviews were conducted in rooms in the clinic, before or after the medical or nursing consultation, by the researchers themselves and by undergraduate students who were involved in the project and properly trained. After the interviews, data on specific risk factors for developing CKD in PLHIV were collected in medical records, such as: Viral load, CD4+ T lymphocyte count, history of DM, SAH and CKD, family history of DM, SAH and CKD, cholesterol, triglycerides, glucose, urea and creatinine tests, time of HIV diagnosis and time on ART.

It is worth mentioning that the creatinine tests, as well as other complementary tests of the clinical follow-up of PLHIV, are part of the routine of Specialized Care Services (SCS) and the Ministry of Health recommends their annual follow-up.[1]

The Nefrocalc 2.0 calculator, available on the website of the Brazilian Society of Nephrology was used to calculate the Glomerular Filtration Rate.[8] The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equa-

tion[9] was used to calculate eGFR. To do this, the conventional creatinine was initially converted to the gold standard isotope dilution mass spectrometry (IDMS) creatinine, in order to minimize its variability.[10]

Renal function impairment was classified by the Adult Glomerular Filtration Rate (GFR) Staging system proposed in the Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease,[11,12] with variations according to age, gender, race, and creatinine. The GFR was classified in six stages, as shown in table 1.[11]

Table 1. Reference values for classification and staging of Glomerular Filtration Rate for adults, according to Kdigo

Glomerular Filtration Rate Stages	
Kidney damage with normal or ↑ GFR	>90 ml/minx1.73m^2 (stage G1)
Mildly Decreased	89-60 ml/minx1.73m^2 (stage G2)
Kidney damage with mild ↓ GFR	59-45 ml/minx1.73m^2 (stage G3a)
Moderate ↓ GFR	44-30 ml/minx1.73m^2 (stage G3b)
Severe ↓ GFR	29-15 ml/minx1.73m^2 (stage G4)
Kidney Failure	<15 ml/minx1.73m^2 (stage G5)

Source: Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO- Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. 2013; Suppl 3:1-150.[11]

Data were processed and analyzed using the Statistical Package for Social Science, version 22.0. Descriptive statistics were used for socio-demographic and clinical characterization of the population. Association tests were performed to verify the association between eGFR and sociodemographic and clinical variables - Chi-square and Fisher's Exact, with p <0.05. The study was authorized by the Municipal Health Department of Ribeirão Preto-SP and by the Research Ethics Committee of the University of São Paulo, in the Ribeirão Preto Nursing School, protocol #794.563/2014. All the participants were assured of the secrecy of the data and of their anonymity. Data was collected after obtaining agreement of the individuals using the Informed Consent Term, following the precepts recommended by the National Health Council, on Resolution 466/12.

Results

Among the 340 participants in the study, 194 (56.2%) were male, 283 (83.2%) were over 30 years old and 155 (44.9%) self-identified as white. In addition, 108 (31.7%) self-identified as smokers, 159 (46.7%) had abnormal BMI at the time of the interview and only 121 (35.5%) engaged in physical exercises. Regarding HIV-related clinical variables, 214 (62.9%) had been diagnosed with HIV infection for more than five years, and 270 (79.4%) had an undetectable viral load at the last examination. The estimated Glomerular Filtration Rate calculated using the CKD-EPI formula identified that 114 (34.1%) presented eGFR ≤ 90 ml/min/1.73m2, of which (90) 27.5% were classified in grade 2, 15 (4.5%) in grade 3A and 07 (2.1%) in grade 3B, as described in table 2.[11]

Table 2. Estimated Glomerular Filtration Rate of People Living with HIV, according to Kdigo (n=340)

Stages	TFG	n(%)	CI 95%
1 – Normal OR high	≥ 90	221(66.0)	61.1 – 70.8
2 – Mildly decreased	60 – 89	92(27.5)	23.1 – 32.1
3A – Mildly to moderately decreased	45 – 59	15(4.5)	2.4 – 6.9
3B – Moderately to severely decreased	30 – 44	7(2.1)	0.6 – 3.8
4 – Severely decreased	15 – 29	-	-
5 – Kidney failure	< 15	-	-

Source: Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO- Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. 2013; Suppl 3:1-150.[11]

There was a greater predominance of males among those with GFR of less than 90 ml/min/1.73m2, but there was a higher prevalence of females among patients who were in stage three (mildly to moderately and moderately to severely decreased). There was a perceptible association between eGFR and the sociodemographic variables gender (p <0.001) and age (p <0.001). Stage 3 renal changes were more prevalent in older adults, showing that the greater the age, the greater the susceptibility to change in renal function, according to data in table 3. Regarding the clinical variables, there was an association between the Glomerular Filtration Rate and the variables SAH (p= 0.004), DM (p <0.001) and BMI (p= 0.012). Regarding the variables related to HIV infection, it was shown that the time of diagnosis had a significant association (p= 0.026) with eGFR.

Table 3. Factors associated with the estimated glomerular filtration rate in people living with HIV (n=340)

Variables	Taxa de Filtração Glomerular ≥90 n(%)	60–89 n(%)	30-59 n(%)	Total	*p-value*
Gender					
Male	134(69.1)	56(28.9)	4(2.1)	194(100.0)	<0.001*
Female	87(61.7)	36(25.5)	18(12.8)	141(100.0)	
Age (in years)					
≤30	48(92.3)	4(7.7)	00(00)	52(100.0)	
30-50	126(67.7)	53(28.5)	7(3.8)	186(100.0)	<0.001†
≥50	47(48.5)	35(36.1)	15(15.5)	97(100.0)	
Race					
White	106(68.4)	42(27.1)	7(4.5)	155 (100.0)	
Black	28(60.9)	14(30.4)	4(8.7)	46(100.0)	0.859†
Asian	9(64.3)	3(21.4)	2(14.3)	14(100.0)	
Brown	77(64.7)	33 (27.7)	9(7.6)	119(100.0)	
Indigenous	1(100.0)	00 (00)	00(00)	1(100.0)	
Arterial hypertension					
Yes	29(53.7)	15 (27.8)	10(18.5)	54(100.0)	0.004†
No	190(68.3)	76 (27.3)	12(4.3)	278(100.0)	
Does not know	2(66.7)	1(33.3)	00(00.0)	3(100.0)	
Diabetes *mellitus*					
Yes	12(41.4)	5(17.2)	12(41.4)	29(100.0)	<0.001*
No	209(68.8)	85(28.0)	10(3.3)	304(100.0)	
Does not know	00(00)	2(100.0)	00(00)	2(100.0)	
Smoking					
Yes	79(73.1)	26(24.1)	3(2.8)	108(100.0)	0.067†
No	142(62.6)	66(29.1)	19(8.4)	227(100.0)	
Body Mass Index (BMI)					
Underweight	12(75.0)	3(18.8)	1(6.2)	16(100.0)	
Normal weight	113(70.6)	42(26.2)	5(3.1)	160(100.0)	
Overweight	61(56.5)	32(29.6)	15(13.9)	108(100.0)	0.012†
Obese	35(68.6)	15(29.4)	1(2.0)	51(100.0)	
Physical Activity					
Yes	78(64.5)	33(27.3)	10(8.3)	121(100.0)	
No	143(66.8)	59(27.6)	12(5.6)	214(100.0)	0.638*
Time of diagnosis (in years)					
≤ 5	89(73.6)	29(24)	3(2.5)	121(100.0)	
> 5	132(61.7)	63(29.4)	19(8.9)	214(100.0)	0.026†
Viral load					
Undetectable	181(67.0)	74(27.4)	15(5.6)	270(100.0)	
> 40	40(61.5)	18(27.7)	7(10.8)	65(100.0)	0.300*

* Chi-Square Test; † Fisher's Exact Test

Discussion

Chronic inflammation related to HIV infection is associated with the onset of various comorbidities, such as renal disease.[3,13] Studies have shown a higher prevalence of renal disease in people living with HIV, when compared to general population.[3,6,14]

According to the socio-demographic characterization in the present study, age was a variable significantly associated with alteration of renal function in PLHIV, supporting the idea that the greater the age, the more susceptible the person will be to renal dysfunction. This finding is confirmed in other national and international studies that describe how the physiological aging process affects renal cells and indicate aging as a risk factor for the progression of CKD.[3,15-17]

There was a higher concentration of more advanced stages of Chronic Kidney Disease (3A and 3B - mildly to moderately decreased and moderately to severe decreased eGFR) among women. These results conflict with other studies that point out male gender as a risk factor for CKD among PLHIV, with a significant decrease in renal function among men.[9,16,18]

It can be inferred that the advanced stages of CKD in women can be attributed to a higher concentration of renal biomarkers in the urine when compared to non-HIV infected women.[19,20] And because they have a longer life expectancy than men, being a woman is considered an independent risk factor for CKD.[20]

Traditionally, factors such as SAH and Diabetes Mellitus are associated with a higher risk of developing kidney disease. Renal impairment is more present among adults living with HIV than among those who do not have the infection.[21,22] SAH and DM share common pathways that interact, and may develop one after another in the same individual.[22] In PLHIV these comorbidities are influenced by the persistence of immune activation and inflammation.[22,23]

Endothelial dysfunction, reduced availability of nitric oxide and activation of the renin-angiotensin-aldosterone system are factors involved in SAH in PLHIV.[22] Diabetes is a factor directly related to hypertension, since hyperglycemia can trigger peripheral vasoconstriction and thus lead to sodium retention.[24]

Studies have shown that HIV infection is independently associated with renal impairment and albuminuria. However, other studies show a greater decline in eGFR and worsening of albuminuria in PLHIV and taking ART, in addition to a higher prevalence of CKD and Terminal Chronic Renal Failure (TCRF).[3,25]

One of the modifiable risk factors for CKD, gain of body weight, should be individually as-

sessed, with close attention to the Body Mass Index (BMI), correcting it when necessary by providing orientations to prevent changes in renal function in PLHIV.

In this study, 46.76% of the participants were classified as overweight. This was significantly associated with eGFR (p = 0.012), in agreement with studies conducted with PLHIV in Brazil and France, in which about 25 to 45% of participants were overweight or obese.[26-28]

In this same context, the antiretroviral therapies affects the body composition and body weight of PLHIV,[28] with lipodystrophy and accumulation of visceral fat.[28-30] Fat distribution is a precursor to metabolic function.[24,31,32] Therefore, obesity may lead to hypertension, dyslipidemia and increased insulin resistance,[24,29,30] increasing the risk factors for altered renal function.[24,32]

Renal diseases associated with HIV and/or with the use of antirretroviral drugs are common subjects in the scientific literature.[32,33] However, studies evaluating renal function in PLHIV on ART and focusing on the anthropometric measurements are still incipient.

In this perspective, the assessment of the nutritional status, fat distribution and body weight of PLHIV is essential for the prevention of health complications and evaluation of the renal function of this population. However, this is a challenge for future studies.

Regarding the specific clinical variables of the HIV infection, the time of diagnosis presented a significant association with eGFR. The presence of CKD among PLHIV is described in the literature, as a common condition in this group.[21]

This finding is in line with studies conducted in the Northeast and South regions of Brazil,[15,16] and with an Italian cohort study,[33] which demonstrated an association between time of exposure to the virus and presence of renal dysfunction.

A cohort study conducted with PLHIV in Spain showed a decline of renal function over time in 1.3% of patients, strengthening evidence on the onset of kidney problems over the years.[34]

Therefore, based on the literature and on the results presented here, the present study reinforces the need to pay close attention and to constant monitor renal function in people living with HIV. In addition, risk factors for CKD should be assessed, with the purpose of monitoring the progression of clinical status and allowing early interventions.

Considering that Chronic Kidney Disease is a long-term disease, has multiple causes and prognostic factors, and can often be asymptomatic,[35] it is necessary to pay attention to modifiable and related risk factors among people living with HIV.

The limitation is related to the type of study, in which a single estimate of Glomerular Filtration Rate was analyzed. Follow-up studies should include a periodic evaluation of renal function to assess the evolution of CKD in PLHIV in clinical-outpatient follow-up at a national level.

Conclusion

The study demonstrated that the variables gender, age, hypertension, diabetes, BMI and time of diagnosis were associated with eGFR. The importance of the complete follow-up of PLHIV is emphasized, as it can prevent the occurrence of renal dysfunction. In addition, these results may contribute to the qualification of nursing care in the Specialized Care Services for PLHIV, since it is necessary to pay close attention to the risk factors for renal disease and, from this new perspective, the nurse can formulate nursing diagnoses, implement pertinent interventions for individual risk factors, and evaluate the results achieved, providing preventive and health promotion actions to improve the quality of life of these people.

Collaborations

Pontes SP, Melo ES, Costa CRB, Antonini M, Sousa LRM, Gir E and Reis RK declare that they participated in the conception and design, data analysis and interpretation, article writing, critical review of the intellectual content and final approval of the version to be published.

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