Scientific Research Publishing

Open Journal of Gastroenterology, 2024, 14, 18-30
https://www.scirp.org/journal/ojgas
ISSN Online: 2163-9469
ISSN Print: 2163-9450

Factors Associated with Renal Impairment in Patients on Tenofovir for Chronic Hepatitis B in Yaoundé (Cameroon)

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How to cite this paper: Ndjitoyap Ndam, A.W., Shu, S.C.E., Maimouna, M., Bekolo Nga, W., Dang Babagna, I., Talla, P., Kowo, M., Ankouane Andoulo, F. and Ashuntantang, G.E. (2024) Factors Associated with Renal Impairment in Patients on Tenofovir for Chronic Hepatitis B in Yaoundé (Cameroon). *Open Journal of Gastroenterology*, **14**, 18-30.
https://doi.org/10.4236/ojgas.2024.141003

Received: December 22, 2023
Accepted: January 21, 2024
Published: January 24, 2024

Abstract

Background: Tenofovir (TFV) is widely used to treat patients with hepatitis B virus (HBV) infection. But kidney abnormalities are the main concern using this drug. Few studies have described the renal impairment due to the TFV in chronic hepatitis B (CHB) in Sub-Saharan Africa. The objective was to evaluate factors associated with renal impairment observed in patients on TFV for CHB. **Method**: It was a hospital based cross sectional prospective study carried out from June 2023 to July 2023 in Yaoundé (Cameroon) and included any patient treated with TFV for CHB during at least a period of 6 months. For each participant, we collected in the medical report socio-demographic data, clinical data, baseline creatinine, treatment information (type of TFV which was Disoproxil Fumarate (TDF) or Alafenamide (TAF), duration). Then, we collected blood samples to measure serum creatinine and phosphate levels and urine dipstick analysis. Factors associated with renal impairment were assessed with the Odds Ratio. A p value of < 0.05 was significant. **Results**: A total of 60 participants were included. The median age was 44 years [36 - 55] and median duration of TFV therapy was 17.5 months [11.7 - 25.7]. The prevalence of reduced eGFR (<60 mL/min/1.73m^2) was 6/60 (10%), the prevalence of hypophosphatemia 6/60 (10%) and the prevalence of albuminuria 24/60 (40%). Factors associated with eGFR reduced were diuretic use (OR 8.5, [1.09 - 9.58], p = 0.042) and duration of TFV ≥ 36 months (OR 34, [4.3 - 266.3], p = 0.001). Those associated with hypophosphatemia

were duration of TFV ≥ 36 months (OR 12.5 [1.88 - 83.3], p = 0.009). While factors associated with albuminuria were TDF prodrug use (OR 8.8 [1.8 - 43.1], p = 0.009), and duration of TFV ≥ 36 months (OR 11.7, [CI 1.3 - 104.5], p = 0.009). **Conclusion**: Kidney function was impaired in some patients receiving TFV for CHB. It should be monitored, particularly after 36 months and for those receiving TDF prodrug.

Keywords

Chronic Hepatitis B, Tenofovir, Factors Associated, Renal Impairment, Cameroon

1. Background

Hepatitis B is a deadly inflammation of the liver caused by the hepatitis B virus (HBV) [1]. Untreated, the infection could lead to liver cirrhosis or hepatocellular carcinoma. The prevalence in Cameroon is estimated to be 11.2%, varying from one region to another [2]. Tenofovir (TFV) is an antiviral widely used in monotherapy to treat patients with hepatitis B virus (HBV) infection [3] [4] [5]. It could be the Tenofovir Disoproxil Fumarate (TDF) at the posology of 300 mg once daily, other the Tenofovir Alafenamide (TAF) 25 mg per day [1]. This last seems to have a lower nephrotoxicity than the first one. The TFV is also prescribed against HIV in an anti-retroviral treatment regimen [6] [7]. The duration of treatment is long, sometimes for life. But kidney abnormalities are the main concern using this drug. Hypophosphatemia is a possible complication in patients. The TFV is associated with a risk of proximal tubular dysfunction and declining estimate glomerular filtration rate (eGFR) [8] [9] [10]. Fanconi syndrome with its complications (bone weakness, dysfunctions in amino acid metabolism and renal lesions) is a possible adverse reaction of TFV treatment, especially in HIV-infected patients [11]. It leads to excessive urinary excretion of solutes handled by the proximal tubule, such as phosphate, glucose, and bicarbonate. Age ≥ 60 years, diabetes mellitus, high blood pressure, and high serum bilirubin have also been described as risk factors for the development of renal insufficiency in chronic hepatitis B (CHB) patients receiving TDF therapy [12]. But, the mechanism of renal impairment in patients with HVB is multifactorial. In addition to the antiviral therapy nephrotoxicity, the kidney disease can be due to the virus itself [13]. The commonest type is membranous glomerulonephritis. Therefore, the monitoring of renal function is recommended during treatment [3] [14]. If there are studies describing renal impairment associated with the use of TFV against HIV in sub-Saharan Africa, few studies have described its effects on renal function in CHB in our area [15] [16] [17].

2. Objective

The objective was to identify factors associated with renal impairment in pa-

tients on TFV for CHB.

3. Materials and Method

A hospital based cross sectional prospective study was carried out over a period of 2 months (June and July 2023) in two referral hepato gastrointestinal units of the Cameroonian capital: Yaoundé General Hospital and Centre Médical la Cathédrale (Yaoundé, Cameroon) and included all consenting patients treated with TFV for CHB during at least 6 months. Patients whose baseline creatinine was not recorded at the start of the treatment were excluded. For each participant, we collected in the medical report socio-demographic data (age, sex), clinical data (BMI, blood pressure readings at rest, comorbidities such as hypertension, diabetes, hepatitis D virus coinfection (HDV), baseline biological characteristics (creatinine, Alanine aminotransferase (ALAT) and Aspartate aminotransferase (ASAT)), treatment (type of TFV which was TDF or TAF, duration of treatment and associated treatment (such as angiotensin receptor blocker (ARB), angiotensin converting enzyme inhibitor (ACEI) and diuretics use). Then, we collected blood samples to measure serum creatinine (to calculate the eGFR) and phosphate levels by spectrophotometry, and midstream urine for dipstick urine analysis.

3.1. Blood Sample and Urine Analysis

1) Serum Creatinine

All samples collected for serum creatinine were centrifuged and stored in the hospital's freezer at −20˚C. We analyzed the samples using a spectrophotometer (HUMAN®). Creatinine was determined using the Jaffe reaction and the GFR is later calculated using the CKD-EPI formula.

2) Serum phosphorus

All samples collected for serum phosphorus were centrifuged and stored in the hospital's freezer at −20˚C. We analyzed the samples using also a spectrophotometer (HUMAN®).

The principle is based on the fact that inorganic phosphate reacts with ammonium molybdate in the presence of sulfuric acid to form a phosphomolybdic complex which is measured at 340 nm. The absorbance at this wavelength is directly proportional to the amount of inorganic phosphorus present in the sample. The procedure described by the fabricant was respected.

3) Dipstick Urine analysis

Urine analysis was realized using a dipstick LABSTIX®. Holding the dipstick at the end opposite to the chemical pads, we dipped it into the freshly collected urine sample for approximately 2 seconds. The dipstick was compared with the colour chart on the dipstick container and each parameter read after its recommended time.

3.2. Data Management and Analysis Plan

At the end of daily data collection, completed forms were assessed, validated,

coded, and stored. Data was entered Access Microsoft and exported Excel. The information was stored on a computer and on an external drive. Data was analyzed according to objectives using the Statistical Package for Social Sciences (SPSS) version 26 and Microsoft Excel.

Renal abnormalities studied were a reduced of eGFR (<60 mL/min/1.73m^2), a hypophosphatemia (Serum phosphorus < 2.5 mg/dL), and an albuminuria (more than 1+ proteinuria on dipstick). Factors associated with renal impairment were assessed with the Odds Ratio (OR). A p-value of < 0.05 was considered significant after bivariate and multivariate analysis.

4. Results

Two hundred and seven (207) files of participants on TFV treatment during at least 6 months for CHB have been recorded during the period. We excluded 101 patients because there was no baseline serum creatinine in their files. After implementing our inclusion criteria, eighty-six participants were eligible to participate in the study for which sixty of them consented to participate.

4.1. Socio Demographic Characteristics of the Study Population

Of the 60 participants, 68.3% (n = 41) were males and the median age [IQR] was 44.0 [36 - 55] years (Table 1).

4.2. Comorbidities in the Study Population

Coinfection with HDV (20 patients, 33.3%), obesity (18 patients, 30%), hypertension (12 patients, 20%), and diabetes mellitus (7 patients, 11.7%) were the most frequent comorbid conditions. We also observed liver cirrhosis (5 patients, 8.3%), HIV (3 patients, 5%), an underweight with BMI < 18 Kg/m^2 (3 patients, 5%) and a hepatocellular carcinoma (1 patient, 1.7%) (Table 1).

4.3. CHB Treatment

The median [IQR] duration of TFV therapy was 17.5 [11.7 - 25.7] months. We noted 53 patients with duration of TFV ≥ 36 months. TDF was the main prodrug observed in 42 patients while TAF was noted in 18 patients.

4.4. Other Medications Used in the Study Population

Herbal African medication (21.7%), angiotensin converting enzyme inhibitors (13.3%) and metformin (11.7%) were the most frequent drugs used. We also noted diuretics (8.3%), angiotensin receptor blocker (8.3%), and non-steroidal anti-inflammatory drugs (6.7%) (Table 1).

4.5. Baseline Biological Characteristics of the Study Population

Of the 60 participants, only 1.7% (1 patient) had a raised serum creatinine at baseline. Until 30 patients (50%) and 29 patients (48.3%) had raised ALAT and ASAT at baseline respectively. We registered 26 patients (43.3%) with Hepatitis

Table 1. Socio demographic characteristics of the study population.

Variable	Category	Frequency (n = 60)	Percentage (%)
Median age[IQR]		44.0 [36 - 55]	
Age groups (years)	[18 - 30]	4	6.7
	[30 - 40]	16	27.7
	[40 - 50]	20	33.3
	[50 - 60[	7	11.7
	≥60	13	21.7
Sex	Male	41	68.3
	Female	19	31.7
Comorbidities	Hepatitis D	20	33.3
	Hypertension	12	20
	Diabetes mellitus	7	11.7
	Liver cirrhosis	5	8.3
	HIV	3	5
	Hepatocellular carcinoma	1	1.7
Medication	Herbal medication	13	21.7
	ACEI	8	13.3
	Metformin	7	11.7
	Diuretics	5	8.3
	ARB	5	8.3
	NSAIDS	4	6.7
Median baseline creatinine [IQR]		0.95 mg/dL [0.80 - 1.10]	
Baseline creatinine	Raised	1	1.7
	Normal	59	98.3
Mean baseline eGFR ± SD		93.18 ± 20.10 mL/min/1.73m^2	
Baseline eGFR	Decreased	1	1.7
	Normal	59	98.3
Median ALAT [IQR]		37.00 IU/L [22.00 - 83.25]	
Baseline ALAT	Raised	30	50
	Normal	30	50
Median ASAT [IQR]		34.00 IU/L [25.50 - 68.75]	
Baseline ASAT	Raised	29	48.3
	Normal	31	51.7
Median baseline viral load [IQR]		1362.00 IU/mL [125.00 - 21642.00]	

ACEI = angiotensin converting enzyme inhibitor, ALAT = alanine aminotransferase, ASAT = aspartate aminotransferase, ARB = angiotensin receptor blocker, HIV = human immunodeficiency syndrome, NSAIDS = non-steroidal anti-inflammatory drugs.

B viral load > 2000 IU/mL (Table 1).

4.6. Renal Function of the Population at Time of the Study

After at least 6 months of TFV treatment, 6 patients (10%) of the participants had an eGFR < 60 mL/min/1.73m^2. There was an increase in mean serum creatinine from baseline (0.95 mg/dL) to after at least 6 months of TFV treatment (1.05 mg/dL) with change in mean serum creatinine being 0.1 mg/dL (p = 0.005) (Figure 1). There was a decrease in mean eGFR from baseline (93.2 mL/min/1.73m^2) to after at least 6 months of TFV treatment (83.6 mL/min/1.73m^2) with change in mean eGFR being 9.6 mL/min/1.73m^2 (p = 0.001) (Figure 1). All 6 participants who had an eGFR < 60 mL/min/1.73m^2 were between the ranges 45 - 59 mL/min/1.73m^2.

The median [IQR] serum phosphorus was 3.3 [2.8 - 3.8] and a total of 6 participants (10%) had hypophosphatemia.

A total of 24 participants (40%) had albuminuria and 5 (20%) were nephrotic range albuminuria (more than 300 mg/dL).

4.7. Factors Associated with Reduced Estimated Glomerular Filtration Rate

In bivariate analysis, factors associated with eGFR reduced were diuretic use (OR 8.5 [1.09 - 9.58], p = 0.042) and duration of TFV ≥ 36 months (OR 34 [4.3 - 266.3], p = 0.001) (Table 2). Sociodemographic characteristics (age and sex),

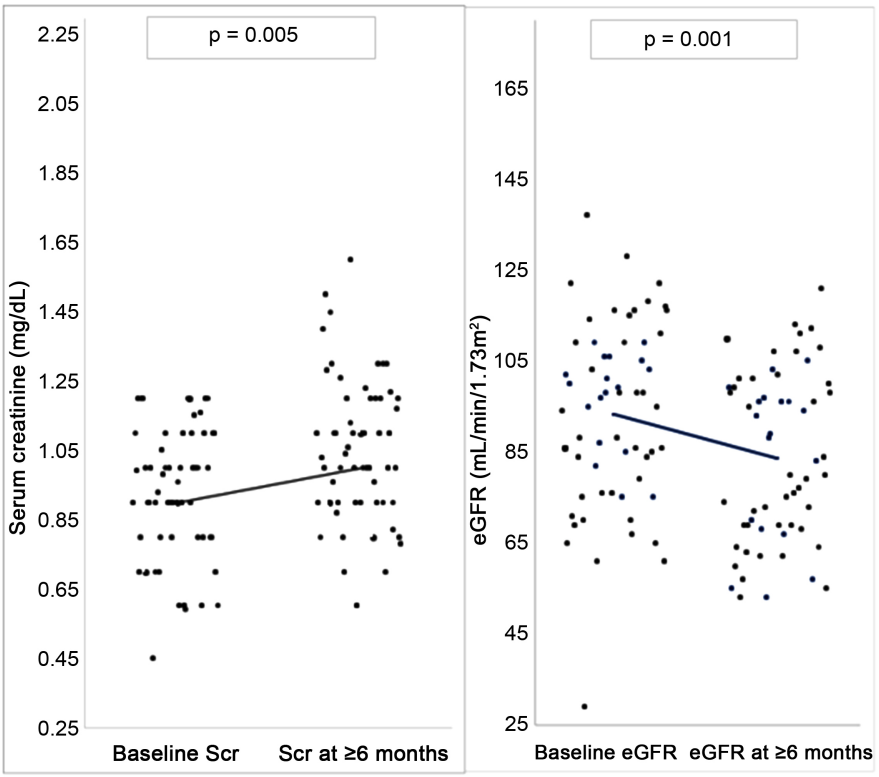

Figure 1. Changes in mean serum creatinine and eGFR of the study population (n = 60).

Table 2. Factors associated with reduced estimated glomerular filtration rate (bivariate analysis) (n = 60).

Variable	Categories	Reduced eGFR		OR (95% CI)	p-value
		Yes (n = 6)	No (n = 54)		
		n (%)	n (%)		
Age (Years)	<60	2 (33.3)	11 (20.4)	1	0.471
	≥60	4 (66.7)	43 (79.6)	1.96 [0.32 - 12.0]	
Sex	Male	3 (50)	38 (70.4)	0.42 [0.08 - 2.31]	0.320
	Female	3 (50)	16 (26.9)	1	
Medication	ARB use	0 (0)	5 (8.4)	Undefined	0.999
	ACEI use	2 (33.3)	6 (11.1)	4.00 [0.60 - 26.68]	0.152
	NSAIDS use	1 (16.7)	3 (5.6)	3.40 [0.30 - 39.10]	0.326
	Diuretics use	**2 (33.3)**	**3 (5.6)**	**8.50 [1.09 - 6.58]**	**0.042**
	Herbal med use	1 (16.7)	12 (22.2)	0.70 [0.07 - 6.58]	0.755
TFV prodrug	TDF	5 (83.3)	37 (40.7)	2.30 [0.25 - 21.2]	0.463
	TAF	1 (16.7)	17 (31.5)	1	
Comorbidities	Hypertension	2 (33.3)	10 (18.5)	2.20 [0.35 - 13.7]	0.399
	Diabetes	0 (0)	7 (13)	Undefined	0.999
	HDV	3 (50)	17 (31.5)	2.18 [0.40 - 1.92]	0.370
BMI (kg/m^2)	<18	1 (16.7)	2 (3.7)	5.20 [0.40 - 7.94]	0.209
	≥18	5 (83.3)	52 (96.3)	1	
Duration of TFV therapy (months)	**<36**	**4 (66.7)**	**3 (5.6)**	**1**	**0.001**
	≥36	**2 (33.3)**	**51 (94.4)**	**34.00 [4.34 - 266.3]**	
ALAT, IU/L	>36	3 (50)	27 (50)	1.00 [0.19 - 5.40]	1.000
	≤36	3 (50)	27 (50)	1	
ASAT, IU/L	>35	3 (50)	26 (48.1)	1.08 [0.20 - 5.82]	0.931
	≤35	3 (50)	28 (51.9)	1	
Hepatitis B viral load, IU/mL	>2000	3 (50)	23 (43.4)	1.30 [0.24 - 7.07]	0.78
	≤2000	3 (50)	30 (56.6)	1	

ACEI = angiotensin converting enzyme inhibitor, ALAT = alanine aminotransferase, ARB = angiotensin receptor blocker, ASAT = aspartate aminotransferase, BMI = body mass index, NSAIDS = non-steroidal anti-inflammatory drugs, TAF = tenofovir alafenamide, TDF = tenofovir disoproxil fumarate, TFV = tenofovir.

comorbidities (hypertension, diabetes mellitus, coinfection with HVD), other medications (ARB use, ACEI use, NSAIDS use, herbal medication use) and baseline biological characteristics (ASAT, ALAT, and HVB viral load) was not associated with eGFR reduced (Table 2). After controlling for cofounders (diuretics use and TFV duration), only the duration of tenofovir therapy of ≥36 months was independently associated with a reduction in estimated glomerular filtration rate (aOR = 56.6, p-value = 0.002). Therefore, this factor increased the risk to have a reduced eGFR.

4.8. Factors Associated with Hypophosphatemia

Factors associated with hypophosphatemia was duration of TFV ≥ 36 months (OR 12.5 [1.88 - 83.3], p = 0.009) (Table 3). Sex, comorbidities (hypertension), medications (ARB use, ACEI use, diuretics use, herbal medication use) and baseline biological characteristics (ASAT, ALAT, and HVB viral load) was not associated with hypophosphatemia (Table 3). Age ≥ 60 years (p = 0.095) and coinfection with HVD (p = 0.089) were marginally associated with hypophosphatemia (Table 3). After controlling for cofounders (age ≥ 60 years, coinfection with HDV, TFV duration), no factor was independently associated with hypophosphatemia.

Table 3. Factors associated with hypophosphatemia (bivariate analysis) (n = 60).

Variable	Categories	Hypophosphatemia		OR [95% CI]	p-value
		Yes (n = 6) n (%)	No (n = 54) n (%)		
Age (Years)	<60	3 (50)	10 (18.5)	1	0.095
	≥60	3 (50)	44 (81.5)	4.4 [0.77 - 25.10]	
Sex	Male	4 (66.7)	37 (68.5)	0.92 [0.15 - 5.51]	0.926
	Female	2 (33.3)	17 (31.5)	1	
Medication	ARB use	0 (0)	5 (9.3)	Undefined	0.999
	ACEI use	1 (16.7)	7 (13.0)	1.34 [0.14 - 13.25]	0.801
	Diuretics use	1 (16.7)	4 (7.4)	2.50 [0.23 - 26.91]	0.450
	Herbal med use	2 (33.3)	11 (20.4)	1.95 [0.32 - 12.09]	0.471
TFV prodrug	TDF	6 (100)	36 (66.7)	Undefined	0.998
	TAF	0 (0)	18 (33.3)	1	
Comorbidities	Hypertension	1 (16.7)	11 (20.4)	0.78 [0.08 - 7.39]	0.830
	HDV	4 (66.7)	16 (29.6)	4.75 [0.79 - 28.60]	0.089
BMI (kg/m^2)	<18	1 (16.7)	2 (3.7)	5.20 [0.40 - 67.94]	0.209
	≥18	5 (83.3)	52 (96.3)	1	
Duration of TFV therapy (months)	**<36**	**3 (50)**	**4 (7.4)**	**1**	**0.009**
	≥36	**3 (50)**	**50 (92.6)**	**12.50 [1.88 - 83.31]**	
ALAT, IU/L	>35	3 (50)	27 (50)	1.00 [0.19 - 5.40]	1.000
	≤35	3 (50)	27 (50)	1	
ASAT, IU/L	>36	3 (50)	26 (48.1)	1.08 [0.20 - 5.82]	0.931
	≤36	3 (50)	28 (51.9)	1	
Hep B Viral load, IU/mL	>2000	2 (33.3)	24 (45.3)	0.60 [0.10 - 3.59]	0.579
	≤2000	4 (66.7)	29 (54.7)	1	

ACEI = angiotensin converting enzyme inhibitor, ALAT = alanine aminotransferase, ARB = angiotensin receptor blocker, ASAT = aspartate aminotransferase, BMI = body mass index, NSAIDS = non-steroidal anti-inflammatory drugs, TAF = tenofovir alafenamide, TDF = tenofovir disoproxil fumarate, TFV = tenofovir.

4.9. Factors Associated with Albuminuria

While factors associated with albuminuria were TDF prodrug use in contrast with TAF prodrug use (OR 8.8 [1.8 - 43.1], p = 0.009), and duration of TFV ≥ 36 months (OR 11.7 [1.3 - 104.5], p = 0.009) (Table 4). Sex, medications (ARB use, ACEI use, Metformin use, NSAIDS use, and diuretics use), comorbidities (hypertension, diabetes mellitus, HDV coinfection), and baseline biological characteristics (ASAT, ALAT, and HVB viral load) was not associated with albuminuria

Table 4. Factors associated with albuminuria (bivariate analysis) (n = 60).

Variable	Categories	Albuminuria		OR (95% CI)	p-value
		Yes (n = 24)	No (n = 36)		
		n (%)	n (%)		
Age (Years)	<60	8 (33.3)	5 (13.9)	1	0.081
	≥60	16 (66.7)	31 (86.1)	3.10 [0.87 - 11.04]	
Sex	Male	14 (58.3)	27 (75)	0.47 [0.15 - 1.41]	0.320
	Female	10 (41.7)	9 (25)	1	
Medication	ARB use			1.00 [0.15 - 6.48]	1.000
	ACEI use	5 (20.8)	3 (8.3)	2.90 [0.62 - 13.48]	0.176
	Metformin use	2 (8.3)	5 (13.9)	0.56 [0.10 - 3.17]	0.516
	NSAIDS use	2 (8.3)	2 (5.6)	1.56 [0.23 - 11.79]	0.326
	Diuretics use	3 (12.5)	2 (5.6)	2.43 [0.37 - 15.58]	0.352
	Herbal med use	8 (33.3)	5 (13.9)	3.10 [0.87 - 11.04]	0.081
TFV prodrug	**TDF**	**22 (91.7)**	**20 (55.6)**	**8.80 [1.80 - 43.15]**	**0.007**
	TAF	2 (8.3)	16 (44.4)	1	
Comorbidities	Hypertension	7 (29.2)	5 (13.9)	2.55 [0.70 - 9.29]	0.155
	Diabetes	2 (8.3)	5 (13.9)	0.56 [0.10 - 3.17]	0.516
	HDV	7 (29.2)	13 (36.1)	0.73 [0.24 - 2.22]	0.577
BMI (kg/m^2)	<18	2 (8.3)	1 (2.8)	3.18 [0.27 - 37.94]	0.356
	≥18	22 (91.7)	35 (97.2)	1	
Duration of TFV therapy	**<36**	**6 (25)**	**1 (2.8)**	**1**	**0.028**
	≥36	**18 (75)**	**35 (97.2)**	**11.7 [1.30 - 104.53]**	
ALAT, IU/L	>36	8 (83.3)	5 (13.9)	1.32 [0.49 - 3.72]	0.598
	≤36	11 (45.8)	19 (58.2)	1	
ASAT, IU/L	>35	12 (50)	17 (47.2)	1.18 [0.40 - 3.12]	0.833
	≤35	12 (50)	19 (52.8)	1	
Hep B Viral load, IU/mL	>2000	12 (50)	14 (40)	1.50 [0.54 - 4.27]	0.448
	≤2000	12 (50)	21 (60)	1	

ACEI = angiotensin converting enzyme inhibitor, ALAT = alanine aminotransferase, ARB = angiotensin receptor blocker, ASAT = aspartate aminotransferase, BMI = body mass index, HDV = hepatitis D virus, NSAIDS = non-steroidal anti-inflammatory drugs, TAF = tenofovir alafenamide, TDF = tenofovir disoproxil fumarate, TFV = tenofovir.

(Table 4). Age ≥ 60 years (p = 0.081) and herbal medication use (p = 0.081) were marginally associated with albuminuria (Table 4). After controlling for co-founders (age ≥ 60 years, herbal medication use, TDF prodrug, TFV duration), only the TDF prodrug use was independently associated with albuminuria (aOR 9.3, p = 0.024). Therefore, this factor increased the risk to have an albuminuria.

5. Discussion

We included 60 patients receiving TFV for CHB since at least 6 months. We observed a male predominance with a median age of 44 years. This male majority has also been described in Cameroon by Halle et al in 2019 [13]. The explanation is probably due to higher risk of HBV and onset of a hepatocellular carcinoma much elevated in men than in women [18]. For this reason, men could be more often on antiviral treatment than women. Our population was relatively young. Jung *et al*. in 2018 in Seoul (South Korea) observed a mean age of 51.3 ± 11.3 years [12]. African patients seem to develop hepatocellular carcinoma younger than those in Asia and West countries [19]. For this reason, in South Saharan Africa we like to prescribe antiviral treatment against HBV early than in Asia and West.

5.1. Mean Changes in Creatinine

At the time of the study, we registered 6 patients (10%) with an elevated serum creatinine in contrast with only one patient before the treatment. This will induce a poor eGFR which is estimated through the serum creatinine. The changes show that the kidney injury is probably due to the antiviral treatment and not due the HBV itself. This results in inferior to 25.4% observed by Yazie *et al*. in 2018 in Ethiopia [10]. This last study was conducted in a population of HIV-patients receiving TFV in combination with other antiretroviral therapy. For this reason, the poly medication could increase the risk of renal injuries.

5.2. Renal Impairment

We observed 6 participants (10%) who had an eGFR < 60 mL/min/1.73m^2. The ranges were between 45 - 59 mL/min/1.73m^2. This value corresponds to a mild kidney injury but which could become severe later if nothing is done [3]. Also, a hypophosphatemia was observed in 6 participants (10%). This could be associated with a proximal tubular dysfunction leading to excessive urinary excretion of phosphate. This abnormality could reveal a Fanconi syndrome [11]. Concerning albuminuria, it was observed in 24 participants (40%) including 5 with a nephrotic range albuminuria (more than 300 mg/dL)! This abnormality is result in glomerular lesions due to the TFV treatment [8]. Without the diagnosis and treatment, this could induce an irreversible chronic kidney disease.

5.3. Factors Associated with Renal Impairment

Duration of TFV therapy ≥ 36 months were associated with a reduced eGFR OR =

34.00 [4.34 - 266.3], p = 0.001; with a hypophosphatemia OR = 12.50 [1.88 - 83.31], p = 0.009 and with a albuminuria OR = 11.7 [1.30 - 104.53], p = 0.028. Diuretics use was associated with a reduced eGFR OR = 8.50 [1.09 - 6.58], p = 0.024; and TDF prodrug use was associated with an albuminuria OR = 8.80 [1.80 - 43.15], p = 0.007. These kidney injuries in patients receiving TDF pro drug and patients receiving the TFV during more than 36 months have also been demonstrated in other studies. TAF compared to TDF demonstrated superiority in the drug effects on several markers of renal (both glomerular and tubular) function and bone turnover [1]. In contrary with some studies, age ≥ 60 years, hypertension and diabetes mellitus were not associated with kidney injuries in our population [12]. The low size of our sample could explain this observation.

6. Limitations of Current Study

Despite our important results, our study has some limitations. We wish to increase the size of the sample with a multicentric analysis and few loss of view. The baseline parameters should be available for everyone. Moreover, our patients had a different duration of treatment. We wish to realize study where all patients are assessed at the same duration of treatment.

7. Conclusion

Kidney function was impaired in some patients receiving TFV for CHB. It should be monitored, particularly after 36 months and for those receiving TDF prodrug.

Acknowledgements

Our study contributes to describing renal impairments observed in patients receiving the Tenofovir for CHB in sub-Saharan country. We analyzed associated factors with these kidney injuries. And we identified the duration of treatment superior to 36 months and the TDF prodrug use as factor increasing risks of these renal dysfunctions.

Declarations Ethics Approval

Ethical clearance number 2023/0779H/UBa/IRB was obtained from the Institutional Review Board of the University of Bamenda (Bamenda, Cameroon). After clear explanation of the study, risk and benefits, only participants who gave their consent were included in the study.

Administrative Authorization

Before the recruitment, we obtained the administrative authorization from the Centre Regional Delegation of Public Health, the general director of the Yaoundé General Hospital and the director of the Centre Médical la Cathédrale.

Consent to Participate

We approached all the patients of our target population and explained the aim

and procedure of the study to them. We further explained the risk and benefits of the study to them. We then requested their consent to participate in the study. Those who accepted to participate gave their consent either verbally or signed the consent form.

Author Contributions

NDJITOYAP NDAM Antonin Wilson, designed the study protocol, wrote the manuscript;

SHU Sonia Charlsia Ewuo, investigator, collected data, wrote the manuscript;

MAIMOUNA Mahamat, analyzed data;

BEKOLO NGA Winnie, reviewed;

DANG BABAGNA Isabelle, collected data;

TALLA Paul, collected data;

KOWO Mathurin, analyzed data;

ANKOUANE ANDOULO Firmin, worked as supervisor;

ASHUNTANTANG Gloria Enow, worked as supervisor.

Competing Interests

Authors state that there are no conflicts of interest.

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