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Gastroenteritis in people living with HIV in Chad: Vulnerability factors and antibiotic resistance

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Abstract

People living with HIV (PLHIV) are vulnerable and often victims of opportunistic infections. Therefore, we undertook a study of gastroenteritis cases among them in four cities (N'Djamena, Kélo, Moundou, Sarh) in Chad. This study involved 648 patients, of whom 63% were former PLHIV on antiretroviral (ARV) therapy for more than 10 years and 37% were newly diagnosed with HIV in an advanced stage of the disease. The main objective of this study was to determine the frequencies of microorganisms associated with gastroenteritis in PLHIV, and secondarily to verify the effectiveness of the most prescribed antibiotics and to identify the adverse effects of the drugs for their management. The isolation and identification of enteropathogenesis in stools were carried out at the laboratory of the National Reference University Hospital Center (CHU-RN), using Hektoen, Mueller-Hinton, EMB, Sabouraud Chloramphenicol media and the API® 20 E gallery. Microscopy, filamentation tests and biochemical tests were used to characterize and determine the rates of parasitic, fungal and bacterial infections, which were 9.6%, 11.3% and 3% respectively. Between long-term (67%) and new (37%) PLHIV, significant differences were observed regarding the adverse effects of antiretroviral therapy (ARV) (vomiting/nausea (p = 0.02), skin rashes (p = 0.001)). Characterization of the susceptibility of the bacterial agents *Salmonella*, *Shigella*, and enterohemorrhagic *Escherichia coli* showed an average resistance rate (76%) to sulfamethoxazole-trimethoprim and nalidixic acid, and 50% resistance to aminopenicillins. On the other hand, an average sensitivity rate of 90% was observed with respect to fluoroquinolones, tetracycline and imipenem. This study not only revealed the characteristics of diarrhea, but also highlighted an effective antibiotic therapy for the prevention of diarrheal diseases in PLHIV in Chad.

Keywords: PLHIV; Diarrhea; Microorganism; Antibiotic; Adverse effect of ARV; Chad

1. Introduction

From 1987 to the present day, Chad has been marked by a significant epidemic of the human immunodeficiency virus (HIV) in the years (2004, 2015, 2020) with prevalences of 3.3%, 1.6%, 1.2% respectively [1]. The adoption of the "test-treat" protocol in 2015, and strong partnerships (Global Fund, UNAIDS) to strengthen access to testing and antiretrovirals, thus reducing new HIV infections and mortality, but the main factors of vulnerability of populations living with HIV are linked to opportunistic infections (tuberculosis, cold, flu, COVID-19, etc.), waterborne diseases (*Escherichia coli*, *Norovirus*, *Rotavirus*, *Cryptosporidium*, *Giardia, Campylobacter*, various serotypes of *Salmonella enterica*, *Shigella* and hepatitis A, leptospirosis and tetanus and *Vibrio cholerae*), conflicts of wars in border countries (Sudan to the East, Libya to the North and Central African Republic to the South) and antiretrovirals (ARV) [2, 3]. In Chad, as elsewhere, adverse effects of antiretroviral drugs (ARV) include digestive disorders (diarrhea, nausea), neurological disorders (headaches, insomnia, dizziness), cutaneous disorders (rashes), and metabolic disorders

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(lipodystrophy, lipid/glycemic disturbances), although newer generations (such as dolutegravir (DTG), tenofovir/lamivudine/dolutegravir (LTD)) are better tolerated, despite recent concerns about weight gain and hypertension. Management involves adjusting the treatment, with regular medical monitoring to prevent serious complications [4]. UNAIDS estimates that 120,000 people are currently living with HIV in the country, but no specific studies have been conducted on gastroenteritis among people living with HIV (PLHIV). The primary objective of this study was to determine the frequency of healthcare-associated microorganisms in PLHIV who had been on antiretroviral therapy (ARV) for more than 10 years and in newly diagnosed PLHIV in four major cities (N'Djamena, Kélo, Moundou, and Sarh) in Chad, and secondarily to assess the effectiveness of antibiotics commonly used in our region to treat PLHIV.

2. Materials and Methods

2.1. Context, period and type of survey

These are prospective and cross-sectional surveys that were carried out from November 3 to December 21, 2025 on the living conditions of people living with HIV (PLHIV) in four cities (N'Djamena, Kélo, Moundou and Sarh) in Chad. Stool samples were collected in sterile containers, and a few grams were then aspirated and transferred to a sterile 5 mL dry tube containing 3 mL of Cary-Blair agar. During the investigation period, the stool samples were kept in a cooler containing a cool box before being transported to the laboratory of the National University Reference Hospital (CHU-RN) in N'Djamena for analysis. A pre-established form containing items (sociodemographic, clinical, paraclinical and therapeutic information) was also used for data collection.

2.2. Study population, Sampling

Volunteer participants (each having signed a consent form) were recruited by convenience sampling at different stages of treatment to search for microorganisms associated with gastroenteritis in people living with HIV, divided into two groups:

- **Group 1:** People living with HIV who had been on antiretroviral therapy for more than 10 years (n=408), aged 19 to 62 years.
- **Group 2:** People newly diagnosed with HIV at an advanced stage of the disease (n=240), aged 11 to 61 years.

2.3. Sample size

Sampling will be random, obtained based on the Cochran formula [5]:

$$N = z^2 p\,(1-p)/I^2$$

N = Sample size
Z = precision level of 1.96 for a 95% confidence level
p = 1.2%: overall HIV seroprevalence 1.2% [6], I = margin of error of 5%
$N = (1.96)^2 \times 0.12\,(1-0.12)/(0.05)^2 = 162$ but given the availability of participants, we continued up to a sample size of 648 stool samples collected.

2.4. Choice of antibiotics

Antibiotics were chosen based on their prescription for the treatment of opportunistic infections in people living with HIV in the different care settings.

Table 1 Antibiotics chosen for the susceptibility test

Category	Family	Antibiotic	Dose/disk
	Beta-Lactams	Amoxicillin (AMX)	25 µg
		Ampicillin (AMP)	10 µg
		Amoxicillin + clavulanic acid (AMC)	20/10 µg
		Ceftriaxone (CRO)	30 µg
		Cefotaxime (CTX)	30 µg

Antibiotic (Bio-Rad)		Imipenem (IMP)	10 µg
	Cyclins	Tetracycline (TET)	30 µg
	Fluroquinolone	Ciprofloxacin (CIP)	5 µg
		Norfloxacin (NXN)	5 µg
	Quinolones	Nalidixic acid (NAL)	30 µg
	Sulfamides	Sulfamethoxazole-trimethoprim (SXT)	1,25 /23,75 µg
	5 famillies	11 antibiotics	

Quality control was performed using the reference strain E. coli ATCC 25922.

2.5. Stool examination

Stool samples were subjected to direct (microscopic) examination for the detection of parasites and yeasts. Aspergillus identification was performed by examining fixed and stained preparations using May-Grünwald-Giemsa (MGG), methylene blue, and Amann's lactophenol (1.44). Lactophenol is particularly useful for washing preparations made in methyl blue. The background is thus decolorized, improving contrast. Furthermore, a colorless background is always advantageous for photomicrography, and the viscosity of lactophenol limits the movement of objects during exposure, which can last several seconds. Examine at 25x and 40x magnification [7].

2.6. Culture and Antibiotic Susceptibility Testing

Isolation and identification of pathogens were performed after inoculation of stool samples onto Hektoen agar, Sabouraud chloramphenicol agar (Bio-Rad®), and EMB (eosin blue methylene) agar. After 18 to 24 hours of incubation in a 37°C incubator, green and bluish colonies with or without a black center on Hektoen agar were suspected (*Salmonella*, *Shigella*), and those with a metallic sheen on EMB agar were also suspected (enteropathogenic *Escherichia coli*). The colonies were sub cultured on to Mueller-Hinton (MH) agar for Gram staining, oxidase testing, and antigenic studies. Biochemical identification was performed using the API® 20 E gallery (Bio-Mérieux 20100). White colonies on Sabouraud chloramphenicol agar are suspected of candidiasis and were sub cultured into 1 mL of human serum and placed in an incubator at 37°C for 24 hours to perform the filamentation test characteristic of *Candida albicans*.

The agglutination test was performed according to the instructions of Kaufmann and White (Pilet et al., 1979) using the following sera: polyvalent anti-*Shigella* type 1, anti-flexneri, anti-*boydii*, and anti-*sonnei* (Bio-Rad®) for the detection of *Shigella*; and anti-*Salmonella* (OMA, OMB, OMC, and Vi) (Bio-Rad®) for the detection of *Salmonella* [8]. For the detection of enteropathogenic *Escherichia coli*, agglutination was performed simply with 0.9% saline to eliminate rough strains, and the identification of *E. coli* serovars was carried out using nonavalent, trivalent, mixture IV, and monovalent agglutination serums. The inoculum was cultured on the API® 20 E gallery (Bio-Merieux 20100) for biochemical identification. The API® 20 E gallery operates on the principle of microtubule inoculum with a suspension that rehydrates the media. Incubation takes place at 37°C in an incubator for 24 hours, during which biochemical reactions (decarboxylation, fermentation, deamination) occur, resulting in spontaneously colored products that are revealed by the addition of reagents. *Salmonella* and *Shigella* were identified using the API® 20 E catalogue. This catalogue provides identification for a large number of profiles obtained using API® 20 E, thus ensuring high reliability in interpreting the results. McFarland 0.5 inoculum was used to perform the antibiogram using standard techniques (disc diffusion method or Kirby-Bauer technique). The diameters of the antibiotic susceptibility discs were read according to the recommendations of the Antibiogram Committee of the French Society for Microbiology [9, 10, 11]

Confirmation of bacterial and fungal strains and antibiogram were performed with the Vitek® 2TM compact 60 automated system. The system includes the Vitek® 2 Compact instrument, a computer (workstation) and a printer. The software supplied with the Vitek® 2 Compact system includes data analysis and management programs. A bidirectional computer interface automatically transfers results to the user's Laboratory Information System (LIS) and to various product and patient reports. A quality control system is available to validate a Vitek® 2 Compact system test kit. An Advanced Expert System™ (AES) (for clinical use) is available to allow systematic online validation of results and interpretation of resistance phenotypes identified by antibiograms. Inoculation preparations for the isolation of bacterial and fungal agents were carried out according to the manufacturer's procedures and standard operating procedures. Using a dispenser, we distributed 3 mL of saline solution (Reference 1204, 500 mL, NaCl 0.45%) into 5 mL tubes arranged in a cassette. Then, using a Pasteur pipette, a colony of the bacteria or yeast was suspended in 3 mL of saline solution, thoroughly mixed, and the optical density was checked with DensiChek McFarland (0.5-0.63) McF for Gram-negative bacteria and 1.80-2.20 McF for yeasts. For each suspension, there is a biochemical identification,

antibiogram, or antifungal susceptibility testing. A Gram (-) V1 221 pipette (0.5–250 µL) was used to dispense 145 µL of identification suspension into 3 mL of saline solution for antibiogram testing (GN = Gram (-) and AST = Corresponding Antibiotic) for each identification. Similarly, for yeasts, a Gram (+) V1 222 pipette (100–1000 µL) was also used to dispense 280 µL of identification suspension into 3 mL of saline solution for antifungal susceptibility testing (YST = yeast identification and YST 10 = corresponding antifungal).

The biochemical identification cards, antibiograms, or antifungal susceptibility testing cards were inserted into the suspensions arranged in the cassette, and the entire assembly was then placed in the Vitek2 analyzer. Once the cassette was in the Vitek2, the loading process was initiated, and the Vitek2 read the barcodes on each card before sealing it. After sealing, the identification cassette was removed, and the Vitek2 performed the analysis. The Vitek2 provides the minimum inhibitory concentration (MIC) of the antimicrobials according to the European Committee for Antimicrobial Susceptibility Testing (ECATET) [11..

2.7. Statistical Analysis

Data were entered and analyzed using Microsoft Word and Excel. The relationship between prevalence and sociodemographic parameters in the study population was assessed using the chi-square test ($p \leq 0.05$). Odds ratios (OR) with 95% confidence intervals were used to determine the degree of association between infection and sociodemographic parameters.

3. Results

3.1. Sociodemographic characteristics of the study population

A total of 648 stool samples were collected from people living with HIV (PLHIV) in four cities (N'Djamena, Kélo, Moundou, and Sarh) in Chad, representing 162 stool samples per location. These samples were analyzed at the bacteriology laboratory of the National University Reference Hospital (CHU-RN) in N'Djamena. Of the 648 PLHIV surveyed, 397 (61%) were women and 251 (39%) were men (p = 0.001, a significant difference), indicating a higher female participation rate in the survey with a sex ratio of 0.63. The mean age of the patients was 36.5 years, ranging from 11 to 62 years.

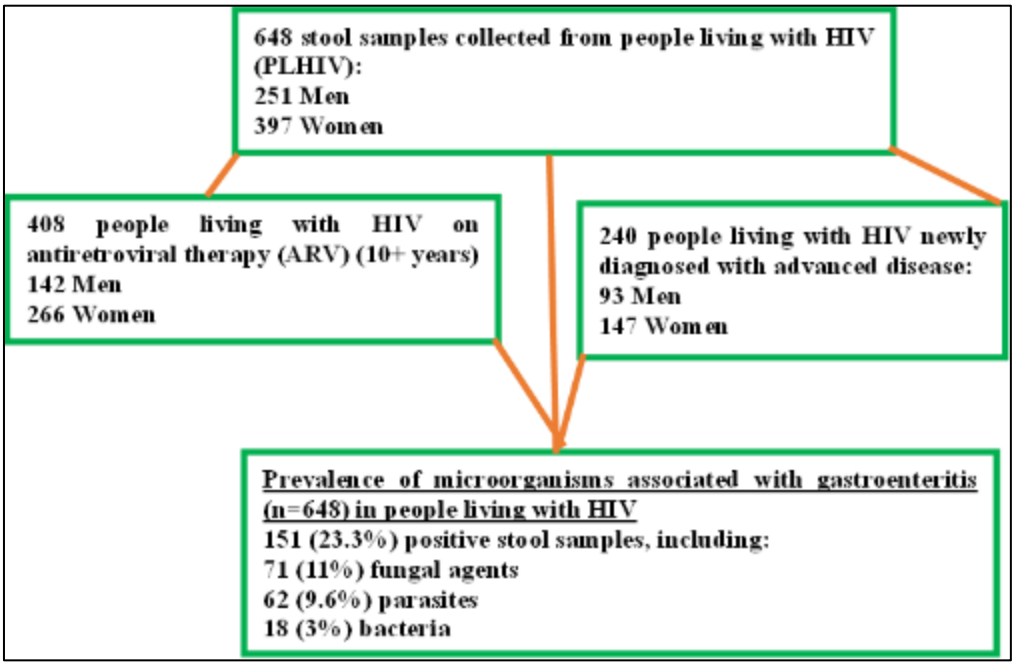

Figure 1 Sociodemographic characteristics of the studied population

3.2. Microbial etiologies of diarrhea and results of the field survey

Of the 648 cultures carried out, 18 (3%) bacterial agents identified, 62 (9.6%) parasitic agents and 71 (11%) fungal agents (yeasts and molds) were found among the 648 stools examined.

Among the 133 parasitic and fungal agents found in the stool samples, 16 (12%) cases of coinfection (bacteria/parasites), 8 (6%) cases of coinfection (bacteria/yeasts), and 6 (4.5%) cases of coinfection (parasites/bacteria/yeasts) were identified. According to the survey, these enteropathogenesis are linked to malnutrition and poor hygiene, generally associated with diarrhea. Furthermore, our study conducted a survey on the most frequently prescribed antibiotics for the management of people living with HIV in Chad (table 1). This survey revealed that Sulfamethoxazole-trimethoprim (SXT: Cotrimoxazole, commonly known as Bactrim) was administered systematically (100%) to all individuals who tested positive for HIV to delay the progression of the disease or to combat opportunistic infections (such as *Salmonella* diarrhea). Aminopenicillins (ampicillin, amoxicillin, amoxicillin + clavulanic acid), ceftriaxone (a third-generation cephalosporin: beta-lactam), and ciprofloxacin (a fluoroquinolone) were widely prescribed, accounting for over 50% of cases in the management of people living with HIV. In most cases, the antibiotic therapy was not tailored to the antibiogram.

3.3. Socio-demographic and clinico-biological characteristics of the studied population according to the presence of microorganisms associated with gastroenteritis

Table 2 shows that 56.3% (long-term HIV-positive individuals on antiretroviral therapy for more than 10 years) had a fasting blood glucose level between 2 and 2.99 g/L (M: 2.9 ± 0.6), and 43.7% (newly diagnosed HIV-positive individuals with advanced disease) had a fasting blood glucose level between 1.6 and 1.9 g/L (M: 2.2 ± 0.32). Regarding dyslipidemia, 31.3% of patients had elevated LDL cholesterol. The mean LDL cholesterol level was 1.2. Patients most affected by infections associated with gastroenteritis and adverse effects of antiretroviral drugs (ARV) were newly diagnosed people living with HIV (PLHIV) with advanced disease, with a mean age of 33.5 years. Significant differences were observed between PLHIV with long-standing (67%) and newly diagnosed (37%) ARV in terms of adverse effects (vomiting/nausea (p = 0.02), skin rashes (p = 0.001)). Overall, by location, of the 151 (23.3%) treated and positive stool samples, Kélo recorded 55 (36.4%) cases, followed by Moundou with 38 (25.2%), N'Djamena with 33 (22%), and Sarh with 25 (16.5%) (table 2).

Table 2 Socio-demographic and clinico-biological characteristics of the study population according to the presence of microorganisms associated with gastroenteritis

Parameter	**Former PLVIs diagnosed while on ART More than 10 years (n=408)**	**Train PELVIs diagnosed while on ART More than 10 years (and=408)**	***P*-value**
Average age (year)	40.5 ± 4.41	36 ± 3.32	0.10
Men (%)	21(14)	64 (31.1)	0.01
Women (%)	19 (13)	47 (42.4)	0.001
Sex-ratio (H/F)	0,53	0.63	0.00
N'Djamena (%)	19 (6.6)	15 (10)	0.00
Kélo (%)	10 (6.6)	45 (30)	0.01
Moundou (%)	17 (11.2)	21 (14)	0.00
Sarh (%)	11 (7.3)	14 (9.3)	0.00
Diarrhea (%)	22 (14.6)	129 (85.4)	0.001
Vomiting/Nausea (%)	24 (16)	127 (84.1)	0.02
Skin rashes (%)	11(7.3)	140 (93)	0.001
Hearing problems (%)	28 (18.5)	123 (81.4)	0.00
BMI (Kg/m^2)	42.03 ± 3.6	27.07 ± 5.9	0.00
Parasites (%)	20 (32.2)	42 (67.7)	0.02
Bacteria (%)	8 (44.4)	10 (55.5)	0.00
Fungal agents (%)	34 (48)	37 (52.1)	0.00
Average Fasting Blood Glucose (g/L)	56.3% (M : *2.9*±0.6 g/L)	43.7% 5 (M: 2.2 ±0.32)	0.00
LDL mean	22.2 (M: 1.*9*±0.6 g/L)	78.8% (M: 1.2g/L±0.5 g/L)	0.00

n = number; % = percentage; BMI = body mass index; LDL = low-density lipoproteins; M = mean.

3.4. Distribution of microorganisms associated with gastroenteritis in people living with HIV by age group

Table 3 shows the distribution of cases according to bacterial, parasitic, and fungal agents. Overall, 151/648 (23.3%) of treated stool samples were positive for all microorganisms (parasites, fungi, and bacteria), and 497 (77%) were negative (p = 0.001, a significant difference favoring negative samples). The results in Table 2 also show that children aged 11 to 20 years and the elderly (51 years and older) were most affected by diarrhea of microbial etiology. A total of 62 parasites (9.6%) were found in the stool. Among them, 13 (21%) *Trichomonas intestinalis*, 15 (24.2%) *Giardia intestinalis*, 7 (11.3%) *Isospora belli*, 14 (22.6%) *Entamoeba histolytica* and (21%) *Schistosoma mansoni*. Eighteen (18) isolated bacterial agents belonged to three genera (*Escherichia*, *Shigella*, *Salmonella*) and to the Enterobacteriaceae family (6 (33.3%) enterohemorrhagic *Escherichia coli*, 4 (22.2%) *Shigella flexneri*, 2 (11.1%) *Salmonella* Typhi, 2 (11.1%) *Salmonella* Typhimurium, 1 (5.5%) *Salmonella* Para Typhi A and 3 (16.6%) *Salmonella arizonae*). Seventy-one (71) fungal agents were found in the stool samples (20 (32.2%) *Candida albicans*, 8 (11.3%) *Candida crusei*, 13 (18.3%) *Candida lipolytica*, 14 (20%) *Cryptococcus laurentii*, 11 (15.5%) *Apergillus niger*, and 5 (7%) *Apergillus fumigratus*). These microorganisms, associated with gastroenteritis with diarrhea and vomiting, were identified either alone in the stool samples or in co-infections (table 3).

Table 3 Distribution of microorganisms associated with gastroenteritis in people living with HIV by age group

Microorganism	**Age range (year)**				
	11-20	**21-30**	**31-40**	**41-50**	**51 et plus**
Parasite					
Entamoeba histolytica	6	2	3	1	2
Giardia intestinalis	4	2	4	2	3
Trichomonas intestinalis	5	-	2	1	5
Isospora belli	-	3	1	2	1
Shistosoma mansoni	1	2	-	3	7
Total (%)	16 (26)	9 (14.5)	10 (16.1)	9 (14.5)	18 (29)
Bacteria					
enterohemorrhagic Escherichia coli	2	-	-	1	3
Shigella flexneri	-	2	1	-	1
Salmonella Typhi	1	1	-	-	-
Salmonella Typhimurium	1	-	-	-	1
Salmonella Para Typhi A	1	-	-	-	-
Salmonella arizonae	-	-	1	-	2
Total (%)	5 (28)	3 (17)	2 (11.1)	1 (5.5)	7 (39)
fungal agent					
Candida albicans	5	2	3	4	6
Candida crusei	2	-	1	3	2
Candida lipolytica	3	2	-	5	3
Cryptococcus laurentii	1	6	2	-	5
Apergillus niger	-	3	-	5	3
Apergillus fumigratus	1	-	2	1	1
Total (%)	12 (17)	13 (18.3)	8 (11.3)	18 (25.3)	20 (28.2)

% = percentage

3.5. Sensitivity and resistance profiles of bacterial strains isolated from the stool of PLHIV

Table 4 shows the susceptibility and resistance profiles of bacterial strains isolated from the stool of people living with HIV (PLHIV) to the tested antibiotics. Resistance of the isolated strains was most pronounced with aminopenicillins. Characterization of the susceptibility of the bacterial agents *Salmonella*, *Shigella*, and enterohemorrhagic *Escherichia coli* showed an average resistance rate (76%) to sulfamethoxazole-trimethoprim and nalidixic acid, and 50% resistance to aminopenicillins. On the other hand, an average sensitivity rate of 90% was observed with respect to fluoroquinolones, tetracycline and imipenem (table 4).

Table 4 Susceptibility and resistance profiles to antibiotics tested on bacterial strains isolated from the stool of PLHIV

ATB	**bacterial strain**											
	***ECEH* (n=6)**		***Shigella flexneri* (n=4)**		***Salmonella* Typhi (n=2)**		***S.* Typhimurium (n=2)**		***S.* Para Typhi A (n=1)**		***S. arizonae* (n=3)**	
	%(R+I)	%**S**	%(R+I)	%**S**	% (R+I)	%**S**	%(R+I)	%**S**	% (R+I)	%**S**	%(R+I)	%**S**
AMP	6 (100)	0(0)	2 (50)	2 (50)	1 (50)	1 (50)	1 (50)	1 (50)	1 (100)	0 (0)	2 (66.7)	1 (33.3)
AMX	4 (66.6)	2 (33.3)	1 (25)	3 (75)	1 (50)	1 (50)	1 (50)	1 (50)	1 (100)	0 (0)	2 (66.7)	1 (33.3)
AMC	2 (33.3)	4 (66.6)	0 (0)	4 (100)	0 (0)	2 (100)	0 (0)	2 (100)	0 (0)	1 (100)	0 (0)	3 (100)
CRO	2 (33.3)	4 (66.6)	1 (25)	3 (75)	1 (50)	1 (50)	0 (0)	2 (100)	1(100)	0 (0)	1 (33.3)	2 (66.7)
CTX	1 (16.6)	5 (83.3)	1 (25)	3 (75)	0 (0)	2 (100)	0 (0)	2 (100)	0 (0)	1 (100)	0 (0)	3 (100)
IMP	1 (16.6)	5 (83.3)	0 (0)	4 (100)	0 (0)	2 (100)	0 (0)	2 (100)	0 (0)	1 (100)	0 (0)	3 (100)
TET	2 (33.3)	4 (66.7)	0 (0)	4 (100)	1 (50)	1 (50)	1 (50)	1 (50)	0 (0)	1 (100)	1 (33.3)	2 (66.7)
CIP	2 (33.3)	4 (66.6)	1 (25)	3 (75)	1 (50)	1 (50)	0 (0)	2 (100)	0 (0)	1 (100)	1 (33.3)	2 (66.7)
NXN	1 (16.6)	5 (83.3)	0 (0)	4 (100)	0 (0)	2 (100)	0 (0)	2 (100)	0 (0)	1 (100)	0 (0)	3 (100)
NAL	4 (66.6)	2 (33.3)	3 (75)	1 (25)	2 (100)	0 (0)	1 (50)	1 (50)	1 (100)	0 (0)	3 (100)	0 (0)
SXT	6 (100)	0 (0)	3 (75)	1 (25)	1 (50)	1 (50)	0 (0)	2 (100)	1 (100)	0 (0)	3 (100)	0 (0)

4. Discussion

In summary, the following question should be answered: do gastroenteritis with diarrhea and vomiting, adverse effects of medications (ARV, antibiotics, etc.), or more generally, the inadequacy of health infrastructure due to diagnostic tools have a negative impact on the health of people living with the human immunodeficiency virus (PLHIV) in Chad?

The answer to this question would certainly require comparing our results between the group of former PLHIV on ARV for more than 10 years and that of new HIV-positive individuals in the advanced stage of the disease with those of other authors could enlighten us, however very little updated data exists on this subject. In our study, infectious diarrhea accounted for 23.3% of cases, including 18 (3%) bacterial diarrhea, 62 (9.6%) parasitic diarrhea, and 71 (11%) fungal diarrheas (yeast and mold) found in the 648 stool samples examined. Among the 133 parasitic and fungal agents found in the stool samples, 16 (12%) cases of coinfection (bacteria/parasites), 8 (6%) cases of coinfection (bacteria/yeast), and 6 (4.5%) cases of coinfection (parasites/bacteria/yeast) were identified. The sex ratio of the two groups of people living with HIV (newly diagnosed and newly diagnosed) was 36.5 years, with the age range being 11 to 62 years, favoring females (61.3%). The most affected age groups were 11 to 20 years and 51 years and older, with high rates of bacterial, parasitic, and fungal infections (table 2). These results show that, in people living with HIV, apart from parasites and fungal agents, the main causes of digestive disorders are bacteria (*Escherichia coli*, *Salmonella* and *Shigella*). These results show that the microbial agents involved in diarrheal diseases are linked to immunosuppression compounded by precarious living conditions and the diet of people living with HIV. Furthermore, Dembélé et al. in Bamako (Mali) found a female predominance, as in our series; Ka *et al*., in Senegal found a mean age of 39.93 years, with extreme ages of 15 and 72 years; and Okomé-Kouakou et al. (Gabon) identified the same causes of diarrhea. The parasitic, fungal and bacterial species identified in this study were: (21%) *Trichomonas intestinalis*, (24.2%) *Giardia intestinalis*, (11.3%) *Isospora belli*, (22.6%) *Entamoeba histolytica* and (21%) *Shistosoma mansoni*. The fungal agents found in the stools were: (32.2%) *Candida albicans*, (11.3%) *Candida crusei*, (18.3%) *Candida lipolytica*, (20%) *Cryptococcus laurentii*, (15.5%) *Apergillus niger* and (7%) *Apergillus fumigratus*. The bacteria isolated were: (33.3%) enterohemorrhagic *Escherichia coli*, (22.2%) *Shigella flexneri*, (11.1%) *Salmonella* Typhi, (11.1%) *Salmonella* Typhimurium, (5.5%) *Salmonella* Para Typhi A and (16.6%) *Salmonella arizonae*) (Table 2). Furthermore, Dembélé et al. in November 2022 found the following results: the most frequently found parasites were *Isospora belli* (33.3%) and *Entamoeba coli* (9.52%). *Salmonella* was the second most common pathogen found in the studies by Dao *et al*., in Mali, Ka *et al*., in Senegal, and Okome et al. in Gabon. Like our series, those by Apetse *et al*., and Okome *et al*., had demonstrated that *Escherichia coli* plays a significant role in the bacterial etiologies of diarrhea in people living with HIV [12, 13, 14].

According to the localities, this study noted a predominance of diarrheal infections for the city of Kélo 55 (36.4%) followed by 38 (25.2%) cases in Moundou, 33 (22%) cases in N'Djamena and 25 (16.5%) cases in Sarh.

In addition to diarrheal diseases, the survey revealed significant differences between the old (67%) and new (37%) PLHIV in the adverse effects of ARV (vomiting/nausea (p = 0.02), skin rashes (p = 0.001) (table 3). The adverse drug reactions observed in this study could be explained by either patient non-adherence to treatment or insufficient follow-up by healthcare professionals, interactions with herbal products or dietary supplements, compounded by the limited healthcare infrastructure in Chad. Many medications can interfere with antiretroviral drugs. Co-formulated bictegravir is contraindicated for co-administration with tuberculosis treatment containing rifampicin or rifabutin. Bictegravir levels fall too low due to the presence of the inducing effect of rifampicin/rifabutin and predispose to the risk of HIV viral insufficiency. Then, our study noted cases of hyperglycemia and hyperlipidemia most among PLHIV who had been receiving ARV treatment for more than 10 years (table 3). Metabolic effects consist of interrelated syndromes of fat redistribution, hyperlipidemia, and insulin resistance. A redistribution of subcutaneous lipids from the face and extremities to the trunk, neck, breasts and abdomen is frequently observed, with an aesthetic effect (called lipodystrophy) which can stigmatize and worry patients. Treating the resulting facial wrinkles with collagen or polylactic acid injections can be beneficial. Weight gain, central obesity, hyperlipidemia, and insulin resistance, which together constitute metabolic syndrome, increase the risk of myocardial infarction, stroke, and dementia. Antivirals of all classes contribute to these metabolic effects, but protease inhibitors are clearly the most implicated. Some older antiretrovirals, such as ritonavir and d4T, are known to have metabolic effects. Others, such as tenofovir disoproxil fumarate, etravirine, atazanavir or darunavir (even when combined with low-dose ritonavir), raltegravir and maraviroc, appear to have little or no effect on lipid levels [15, 16, 17]. Finally, our study surveyed the most frequently prescribed antibiotics for the management of people living with HIV in Chad (table 1). This survey revealed that Sulfamethoxazole-trimethoprim (SXT: Cotrimoxazole, commonly known as Bactrim) was administered systematically (100%) to all individuals who tested positive for HIV, either to delay the onset of the disease or to combat opportunistic infections (such as *Salmonella* diarrhea). Aminopenicillins (ampicillin, amoxicillin, amoxicillin + clavulanic acid), ceftriaxone (a third-generation cephalosporin: beta-lactam), and ciprofloxacin (a fluoroquinolone) were widely prescribed,

accounting for over 50% of cases in the management of people living with HIV (PLHIV). In most cases, the antibiotic therapy was not tailored to the antibiogram. Ciprofloxacin was the most frequently used antibiotic for bacterial diarrhea, representing 34.80% of cases. It was used primarily to treat diarrhea caused by *Escherichia coli*. There was no statistically significant relationship between isolated bacteria and the antibiotics used for bacterial diarrhea (*p* greater than 0.05) [18]. In light of the results of the survey on antibiotic therapy, which was mostly non-probabilistic, an evaluation of the efficacy of the identified antibiotics (table 1) was carried out, the results of which are recorded in Table 4.)). Characterization of the susceptibility of the bacterial agents *Salmonella*, *Shigella*, and enterohemorrhagic *Escherichia coli* showed an average resistance rate (76%) to sulfamethoxazole-trimethoprim and nalidixic acid, and 50% resistance to aminopenicillins. On the other hand, an average sensitivity rate of 90% was observed with respect to fluoroquinolones, tetracycline and imipenem (table 4). This increase in resistance is thought to be due to the inappropriate and abusive prescribing practices observed by healthcare workers during our investigation. Cross-resistance was also observed in this family, with 6 (100%) enterohemorrhagic *Escherichia coli* developing resistance to ampicillin due to amoxicillin misuse, which in turn led to 4 (77%) enterohemorrhagic *Escherichia coli* developing cross-resistance to amoxicillin. Such resistance, when observed, is thought to be linked to the production of penicillinase-like beta-lactamases by the strain in question (Yandai et al., 2014; Africa CDC, 2020) [19,20].. Our results could be explained by this phenomenon. This sensitivity was also observed by Dembélé et al. (2022), Salah et al. (2017), and Reinheimer et al. (2017) [20, 21].

5. Conclusion

People living with HIV (PLHIV) are a vulnerable group. They are victims of infectious diseases caused by parasites, fungi, and bacteria involved in diarrheal diseases, thus highlighting a public health problem posed by these microorganisms among people living with HIV in Chad. These enteropathogenic diarrheal diseases are due to the general prevalence of infections linked to the socioeconomic conditions of PLHIV. Furthermore, the isolated bacterial strains are much more resistant to antibiotics (sulfamethoxazole-trimethoprim (cotrimoxazole), ampicillin, amoxicillin, nalidixic acid), further complicating the situation. The most susceptible antibiotics are ciprofloxacin, norfloxacin, tetracycline, and imipenem. Furthermore, this study highlighted the prevalence and frequency of enteropathogens in the stool of people living with HIV (PLHIV), linked to their diet and poor hygiene, which are generally associated with diarrheal diseases. Controlling these infections requires a concerted effort among various stakeholders (governments, basic humanitarian services, and PLHIV).

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflicts of interest.

Statement of ethical approval

To conduct this study, we obtained:

Before conducting this study, we obtained:

- Research authorization from the Dean of the Faculty of Human Health Sciences, University of N'Djamena, Chad;
- Research authorization from the Director General of the Ministry of Public Health of Chad;
- Research authorization from the Director of the National University Referral Hospital Center of N'Djamena, Chad.

Statement of informed consent

- Written and signed consent was obtained from each patient or their legal representative, to whom we explained the procedures and the importance of the study;

- In accordance with medical ethics and in order to preserve the moral integrity and confidentiality of the patients, we ensured anonymity;
- The results of our research were shared with clinicians for patient care.

Author Contributions

BN participated in the study design and provided supervision, as well as critical review and editing of the manuscript. AM and DA contributed to data collection and laboratory analysis. All authors read and approved the final version of the manuscript.

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