


## Original Investigation

# Effect of HIV Infection and Highly Active Antiretroviral Therapy on Hearing Function

## A Prospective Case-Control Study From Cameroon

Jean Valentin F. Fokouo, MD; Jean Espoir E. Vokwely, MD; Jean Jacques N. Noubiap, MD; Brice Enid Nouthé, MDCM, MSc; Joseline Zafack, MD, MPH; Esthelle Stéphanie Minka Ngom, MD; Asmaou Bouba Dalil, MD; Adèle-Rose Ngo Nyeki, MD; Géneviève Bengono, MD; Richard Njock, MD

 Supplemental content at [jamaotolaryngology.com](http://jamaotolaryngology.com)

**IMPORTANCE** Human immunodeficiency virus (HIV) infection remains a major cause of morbidity and mortality worldwide. Many studies have found a higher prevalence of hearing impairment among HIV-positive individuals.

**OBJECTIVE** To investigate the effect of HIV and highly active antiretroviral treatment (HAART) on the hearing function in a Cameroonian population.

**DESIGN, SETTING, AND PARTICIPANTS** We conducted a prospective case-control study from March 1, 2012, through January 31, 2013. The study took place at the National Social Insurance Fund Hospital in Yaoundé, Cameroon, a public health facility. We included 90 HIV-positive case patients and 90 HIV-negative control patients aged 15 to 49 years without any history of hearing loss or treatment with a known ototoxic drug. The case group was further divided into 3 subgroups: 30 HAART-naïve patients, 30 patients receiving first-line HAART, and 30 patients receiving second-line HAART.

**INTERVENTIONS** Hearing function was assessed by pure-tone audiometry and classified according to the criteria of the Bureau International d'Audio-Phonologie.

**MAIN OUTCOMES AND MEASURES** Hearing loss due to HIV and HAART.

**RESULTS** The HIV-positive patients had more otologic symptoms (hearing loss, dizziness, tinnitus, and otalgia) than HIV-negative patients (41 vs 13,  $P = .04$ ). There were 49 cases (27.2%) of hearing loss in the HIV-positive group vs 10 (5.6%) in the HIV-negative group ( $P = .04$ ). Compared with HIV-negative individuals, the odds of hearing loss were higher among HIV-infected HAART-naïve patients (right ear: odds ratio [OR], 6.7; 95% CI, 4.3-9.7;  $P = .004$ ; left ear: OR, 6.2; 95% CI, 3.5-8.3;  $P = .006$ ), patients receiving first-line HAART (right ear: OR, 5.6; 95% CI, 1.9-10.5;  $P = .01$ ; left ear: OR, 12.5; 95% CI, 8.5-15.4;  $P < .001$ ), and patients receiving second-line HAART (right ear: OR, 6.7; 95% CI, 3.3-9.6;  $P = .004$ ; left ear: OR, 3.7; 95% CI, 3.0-5.0;  $P = .08$ ).

**CONCLUSIONS AND RELEVANCE** Hearing loss is more frequent in HIV-infected patients compared with uninfected patients. Therefore, HIV-infected patients need special audiologic care. Further studies are needed because controversy remains regarding the factors that lead to ear damage.

*JAMA Otolaryngol Head Neck Surg.* 2015;141(5):436-441. doi:10.1001/jamaoto.2015.125  
Published online March 5, 2015.

**Author Affiliations:** Author affiliations are listed at the end of this article.

**Corresponding Author:** Jean Valentin F. Fokouo, MD, Department of Medicine and Biomedical Sciences, University of Yaoundé I, c/o Dietagoum Madjouka Stephanie, PO Box 8460, Yaoundé, Cameroon.

According to the Gap Report published in 2014 by the Joint United Nations Program for HIV/AIDS, 35 million persons were living with human immunodeficiency virus (HIV) at the end of 2013, of whom 24.7 million (71%) lived in sub-Saharan Africa.<sup>1</sup> Currently, access to highly active antiretroviral therapy (HAART) not only promotes a longer life but also leads to an increase of diseases that had previously been underreported. There is growing concern among scientists about the deleterious effects of HIV and antiretroviral (ARV) drugs on the ear. From 40% to 90% of HIV-positive patients will experience otolaryngologic conditions during the course of their disease.<sup>2-4</sup> The frequency of these conditions is approximately twice as high in the HIV-positive population compared with the HIV-negative population.<sup>5</sup> Hearing loss has been reported in approximately 20% to 50% of patients with HIV.<sup>6-8</sup> According to the National Institutes of Health, as many as 75% of adults with AIDS have some kind of hearing disorder.<sup>9</sup> Many hearing disorders are due to a higher incidence of ear disease from HIV itself or from opportunistic infections and ototoxic drugs.<sup>6</sup>

Sub-Saharan Africa is home to the most HIV-positive people in the world,<sup>10</sup> yet most studies on HIV infection originate in developed countries. Reviews from Assuiti et al<sup>11</sup> and Mrema<sup>12</sup> found a unanimously higher incidence of hearing loss in patients with HIV, although no strong relation with any specific factor could be drawn. In South Africa, investigators studied the ototoxicity of ARV drugs and HIV.<sup>7,13,14</sup> They confirmed the abovementioned findings and emphasized the need for closer monitoring of hearing in patients with HIV undergoing HAART.<sup>13</sup> Since May 2007 in Cameroon, HAART has been available free of charge nationwide.<sup>15,16</sup> In 1997, Bengono et al<sup>17</sup> found that 21.7% of HIV-infected Cameroonian patients had otologic manifestations. Moreover, studying inaugural manifestations of HIV in 2002, Ndjolo et al<sup>18</sup> found that 11.5% of patients discovered their HIV status after an otolaryngologic event. However, no study has examined the effect of HIV and HAART on hearing in Cameroon. Therefore, this study aimed to assess the effect of HIV and HAART on hearing function.

## Methods

We conducted a prospective case-control study in patients aged 15 to 49 years in the National Social Insurance Fund Hospital in Yaoundé, Cameroon, from March 1, 2012, through January 31, 2013. The HIV-positive patients (cases) were selected from the registered center for treatment of patients with HIV; the ear, nose, and throat service; outpatient clinics; or the Department of Internal Medicine. The HIV test was performed in 2 steps. A rapid test (Determine; Inverness) was first performed. If the result was positive, a confirmatory test was performed using enzyme-linked immunosorbent assay or Western blot. The HIV-negative patients were selected from outpatient clinics or laboratories after a negative HIV test result. In addition, we excluded any patient with a medical history of treatment with traditional medicine or a known ototoxic drug (eg, aminoglycosides, diuretics, quinine, cytotoxic agents, and antituberculosis agents) taken less than 3 months

before the study, a family history of deafness, occupational exposure to noise, ear surgery, and any condition leading to deafness by itself or its treatment (eg, syphilis, tuberculosis, otitis, meningitis, stroke, cancer, pneumocystosis, neuromeningeal cryptococcosis, diabetes, hypertension, and ear surgery). We performed an otolaryngologic examination with otoscopy. We then performed pure-tone audiometry (PTA) in a soundproof box, looking for the thresholds from frequencies of 125 to 8000 Hz on air conduction (AC) and 250 to 8000 Hz on bone conduction (BC) with the A33 device (Interacoustics). The pure-tone average was calculated and classified according to the criteria of the Bureau International d'Audio-Phonologie (BIAP).<sup>19</sup> We recruited a total of 180 patients, 90 of whom were HIV negative (controls) and 90 of whom were HIV positive (cases). The latter were divided into 3 subgroups: 30 HAART-naïve patients, 30 patients receiving first-line HAART, and 30 patients receiving second-line HAART. The first- and second-line HAART regimens are defined by the World Health Organization guidelines<sup>20</sup> and applied by National Aids Control Committee registered treatment centers. The first-line regimens were fixed-dose combinations made from 3 of the following compounds: lamivudine, zidovudine, efavirenz, tenofovir disoproxil fumarate, and nevirapine. The second-line regimens, in addition to the abovementioned elements (minus efavirenz and nevirapine), could add abacavir sulfate, ritonavir-boosted lopinavir, or didanosine in a tri-therapy. The distribution of HAART regimens is given in the eTable in the Supplement.

The protocol of this study was approved by the Ethics Committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I. Each patient or parent provided a signed, written informed consent form to participate in the study.

The data collected were analyzed with SPSS statistical software, version 14 (SPSS Inc). The *t* test,  $\chi^2$  test, and Kruskal-Wallis test were used to compare means between the subgroups. Univariate analysis was used to study the effect of age, sex, CD4 cell count, and duration of treatment on hearing. Odds ratios (ORs) were used to compare the susceptibility of hearing impairment among the subgroups. *P* < .05 was considered statistically significant.

## Results

We recruited 180 patients (360 ears), 129 (71.7%) of whom were women (60 HIV-negative women, 22 HAART-naïve women, 23 receiving first-line HAART, and 24 receiving second-line HAART). The mean (SD) age was 33.4 (7.7) years, with a breakdown of 35.3 (7.8) years in the HIV-positive group and 31.5 (7.2) years in the HIV-negative group.

HIV-positive patients had more otologic symptoms than HIV-negative patients (41 vs 13; *P* = .04), including vertigo (5 vs 3), tinnitus (18 vs 5), otalgia (5 vs 0), and hearing loss (13 vs 5). The general characteristics of the cases are given in Table 1.

The PTA data revealed 49 cases (27.2% of ears) of hearing loss in the HIV-positive group vs 10 (5.6%) in the HIV-negative group (*P* = .04). The hearing loss was left-sided in

**Table 1. General Characteristics of the HIV-Positive Patients<sup>a</sup>**

Characteristic	HAART-Naive Patients (n = 30)	Patients Receiving First-Line HAART (n = 30)	Patients Receiving Second-Line HAART (n = 30)	Total HIV-Positive Patients (n = 90)
HIV duration since discovery, y				
<1	19 (63.3)	1 (3.3)	1 (3.3)	21 (23.3)
1-5	9 (30.0)	18 (60.0)	17 (56.7)	44 (48.9)
>5	2 (6.7)	11 (36.7)	12 (40.0)	25 (27.8)
HIV type				
Unknown	19 (63.3)	16 (53.3)	14 (46.7)	49 (54.4)
Type 1	11 (36.7)	13 (43.3)	16 (53.3)	40 (44.4)
Type 2	0	1 (3.3)	0	1 (1.1)
CD4 cell count range				
<200	16 (53.3)	3 (10.0)	7 (23.3)	26 (28.9)
200-499	12 (40.0)	19 (63.3)	15 (50.0)	46 (51.1)
≥500	2 (6.7)	8 (26.7)	8 (26.7)	18 (20.0)
WHO stage				
I	10 (33.3)	3 (10.0)	5 (16.7)	18 (20.0)
II	10 (33.3)	16 (53.3)	13 (43.3)	39 (43.3)
III	9 (30.0)	11 (36.7)	12 (40.0)	32 (35.6)
IV	1 (3.3)	0	0	1 (1.1)
Duration of HAART, y				
<1	NA	3 (10.0)	2 (6.7)	5 (5.6)
1-5	NA	19 (63.3)	17 (56.7)	36 (40.0)
>5	NA	8 (26.7)	11 (36.7)	19 (21.1)
CD4 cell count, mean (SD), /μL	205 (182)	431 (268)	394 (270)	343 (260)

Abbreviations: HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; NA, not applicable; WHO, World Health Organization.  
 SI conversion factor: To convert CD4 cell counts to ×10<sup>9</sup>/L, multiply by 0.001.  
<sup>a</sup> Data are presented as number (percentage) of patients unless otherwise indicated.

**Table 2. Hearing Level According to BIAP Classification**

Study Group	Hearing Loss											
	Normal Hearing (≤20 dB)		Mild (21-40 dB)		Moderate (41-70 dB)		Severe (71-90 dB)		Profound (91-119 dB)		Cophosis (≥120 dB)	
	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE
HIV negative	86	84	4	4	0	1	0	1	0	0	0	0
HAART naive	22	23	7	7	1	0	0	0	0	0	0	0
First-line HAART	23	18	6	11	0	1	0	0	0	0	1	0
Second-line HAART	22	23	7	4	1	2	0	1	0	0	0	0

Abbreviations: BIAP, Bureau International d'Audio-Phonologie; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; LE, left ear; RE, right ear.

**Table 3. Comparison of Patient Groups According to Pure-Tone Average**

Study Group	Right Ear			Left Ear		
	No. of Patients	Pure-Tone Average, Mean (SD)	P Value <sup>a</sup>	No. of Patients	Pure-Tone Average, Mean (SD)	P Value <sup>a</sup>
HIV negative	90	13.2 (5.0)	Reference	90	12.4 (9.6)	Reference
HAART naive	30	19.3 (11.0)	.006	30	17.0 (8.5)	.02
First-line HAART	30	20.2 (20.2)	.003	30	18.8 (10.0)	.002
Second-line HAART	30	17.0 (9.3)	.04	30	18.7 (13.5)	.006

Abbreviations: HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus.

<sup>a</sup> Determined by t test.

43.0% of cases, right-sided in 21.0%, and bilateral in 36.0%. Sensorineural hearing loss was predominant (61.7%), followed by mixed hearing loss (20.0%) and conductive hearing loss (18.3%). The BIAP classification of the hearing loss is given in **Table 2**. The comparison of pure tone averages in AC and BC is given in eFigures 1 and 2 in the Supplement for the right and left ear,

respectively. The comparison reveals the gaps between the cases and controls in the frequency range. **Table 3** demonstrates a statistically significant increase in pure tone averages in HIV-positive patients (HAART-naive patients and patients receiving first- and second-line HAART) when compared with the HIV-negative patients. They had pure-tone averages

**Table 4. Characteristics of Patients With Moderate to Profound Hearing Loss**

Patient No./ Sex/Age, y	Study Group	Side <sup>a</sup>	WHO Stage	Symptom	Severity of Hearing Loss	HIV Duration Since Discovery, y	CD4 Cell Count, / $\mu$ L	Pure-Tone Average, dB	HAART Regimens
1/M/38	HAART naive	Right	III	Hearing loss, ear pruritus	Moderate	1-5	255	56.2	None
2/F/24	First-line HAART	Right	III	Tinnitus, hearing loss	Profound	1-5	191	120.0	Lamivudine, zidovudine, and nevirapine
3/F/38	Second-line HAART	Both	III	None	Moderate	>5	650	41.2	Lamivudine, zidovudine, and lopinavir-ritonavir
4/F/36	First-line HAART	Left	III	Tinnitus	Moderate	>5	400	45.0	Lamivudine, zidovudine, and nevirapine
5/F/32	Second-line HAART	Left	III	Hearing loss	Severe	1-5	168	75.0	Tenofovir, lamivudine, and lopinavir-ritonavir
6/F/30	Second-line HAART	Left	II	None	Moderate	1-5	1076	41.2	Tenofovir, lamivudine, and lopinavir-ritonavir

Abbreviations: HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; WHO, World Health Organization.

SI conversion factor: To convert CD4 cell counts to  $\times 10^9/L$ , multiply by 0.001.

<sup>a</sup> Side of affected ear: right, left, or both.

**Table 5. Odds Ratios (ORs) for the Probability of Having Abnormal Hearing on Pure-Tone Audiometry<sup>a</sup>**

	Severity of Hearing Loss, No. (%)				OR (95% CI)	P Value
	Normal	Mild	Moderate	Profound		
<b>Right ear</b>						
HIV negative (n = 90)	86 (95.6)	4 (4.4)	0	0	1 [Reference]	
HAART naive (n = 30)	22 (73.4)	7 (23.3)	1 (3.3)	0	6.7 (4.3-9.7)	.004
First-line HAART (n = 30)	23 (76.7)	6 (20.0)	0	1 (3.3)	5.6 (1.9-10.5)	.01
Second-line HAART (n = 30)	22 (73.4)	7 (23.3)	1 (3.3)	0	6.7 (3.3-9.6)	.004
<b>Left ear</b>						
HIV negative (n = 90)	84 (93.4)	4 (4.4)	1 (1.1)	1 (1.1)	1 [Reference]	
HAART naive (n = 30)	23 (76.7)	7 (23.3)	0	0	6.2 (3.5-8.3)	.006
First-line HAART (n = 30)	18 (60.0)	11 (36.7)	1 (3.3)	0	12.5 (8.5-15.4)	<.001
Second-line HAART (n = 30)	23 (76.7)	4 (13.3)	2 (6.6)	1 (3.3)	3.7 (3.0-5.0)	.08

Abbreviations: HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus.

<sup>a</sup> Profound hearing loss, severe hearing loss in the right ear, and profound hearing loss in the left ear were removed from the comparison because no patients presented with these conditions.

of 19.3 dB ( $P = .006$ ), 20.2 dB ( $P = .003$ ), and 17.0 dB ( $P = .04$ ) vs 13.2 dB in the HIV-negative group for the right ear and 17.0 dB ( $P = .02$ ), 18.8 dB ( $P = .002$ ), and 18.7 dB ( $P = .006$ ) vs 12.4 dB in the left ear.

On univariate analysis, the age, sex, CD4 cell count, and duration of HAART did not significantly influence hearing loss. Six HIV-positive patients had moderate to profound hearing loss; their characteristics are summarized in **Table 4**. All had been diagnosed as having hearing loss for more than 1 year, and 3 were receiving second-line HAART. No significant difference was found in terms of pure tone averages and susceptibility to hearing loss between HAART-naive patients and those receiving HAART. The HIV-positive subgroups had a greater chance of hearing loss than the HIV-negative controls for the HAART-naive patients (right ear: OR, 6.7; 95% CI, 4.3-9.7;  $P = .004$ ; left ear: OR, 6.2; 95% CI, 3.5-8.3;  $P = .006$ ), patients undergoing first-line HAART (right ear: OR, 5.6; 95% CI, 1.9-10.5;  $P = .01$ ; left ear: OR, 12.5; 95% CI, 8.5-15.4;  $P < .001$ ), and patients undergoing second-line HAART (right ear: OR, 6.7; 95% CI, 3.3-9.6;  $P = .004$ ; left ear: OR, 3.7; 95% CI, 3.0-5.0;  $P = .08$ ). In the left ear, patients undergoing second-line HAART had the same risk of hearing loss as the controls (**Table 5**).

## Discussion

There is a gap in the recognition of hearing impairment among HIV-infected patients in Sub-Saharan Africa. This study aimed to better understand the influence of both HIV and HAART on hearing in a Cameroonian population. We discovered that HIV-positive patients had poorer hearing on PTA than that of HIV-negative patients. The HIV-positive patients had significantly more symptoms of hearing loss, tinnitus, and dizziness and less chance than their HIV-negative counterparts to have normal hearing. However, when the HIV-positive subgroups were compared, no significant differences were found between them. The age, sex, CD4 cell count, and duration of HAART did not affect hearing.

The otologic symptoms (otalgia, hearing loss, tinnitus, and dizziness) were more frequent in the HIV-positive group than in the HIV-negative group ( $P = .04$ ). This tendency was also found by Mata Castro et al<sup>5</sup> and Wang et al.<sup>8</sup> Chandrasekhar et al<sup>21</sup> found ear fullness (34%), tinnitus (26%), hearing loss (29%), otalgia (23%), and otorrhea (5%). They also found auditory disease to be affecting up to 33% of HIV-

infected patients and sensorineural hearing loss to be more severe in this specific group. We found hearing loss to be significantly more frequent among HIV-positive patients compared with HIV-negative controls (27.2% vs 5.6%). In contrast, Khoza-Shangase<sup>14</sup> and Marra et al<sup>22</sup> found only 10%. The difference lies in their definition of deafness, which they considered to be any hearing threshold elevation equal or superior to 25 dB. The BIAP criteria used in the current study sets the threshold as low as 21 dB, thus allowing more patients to fall into this category. Our findings support the fact that patients with HIV have more otologic manifestations.

Hearing loss was bilateral in 43.0% of cases, left-sided in 36.0%, and right-sided in 21.0%. To date, we have no explanation for this left-sided predominance, which was also found by Khoza-Shangase.<sup>14</sup> In fact, ototoxicity can also lead to unilateral hearing loss.<sup>23</sup> As for the severity of hearing loss, 42 (85.7%) of 49 patients in the HIV-positive group and 8 (80%) of 10 patients in the HIV-negative group had mild hearing loss. All 6 patients with moderate to profound hearing loss had their conditions diagnosed more than 1 year before the study and were in advanced stages of the disease. Regarding the type of hearing loss, there was a predominance of sensorineural hearing loss (61.7%). Some authors had the same results,<sup>2,8,13,21,24</sup> and van der Westhuizen et al<sup>25</sup> found the same proportions in a similar study in South Africa. These outcomes can be explained by the neurotropism of HIV,<sup>3,26</sup> the probable toxic effects of ARV drugs on ears,<sup>11</sup> or by drugs that are used against opportunistic infections.<sup>27</sup> In fact, Marra et al<sup>22</sup> found that, in patients older than 35 years, there was a greater risk of hearing loss linked to HAART. According to these investigators, nucleotide reverse transcriptase inhibitors cause damage in the mitochondrial DNA in the inner ear, which accumulates over time and finds expression in older patients. However, other authors discovered a predominance of conductive hearing loss in adults<sup>2</sup> or children<sup>6</sup> as a result of eustachian tube issues secondary to nasopharyngeal infections or tumors.

The ORs indicate that all 3 HIV-positive subgroups had a lessened chance to have normal hearing than the controls on both ears, except the patients undergoing second-line HAART on the left ear, who had no significant difference with the controls. Age, sex, duration of disease or treatment, and CD4 cell count had no association with hearing loss in logistical regression analyses. However, these results are not conclusive because the comparison lacked power due to the small sample. This aspect must be further studied in larger samples.

The pure tone averages were significantly higher in the HIV-positive subgroups, especially in the higher frequency on AC and BC in both ears. Obasikene et al<sup>28</sup> had similar results in a Nigerian study of ototoxicity in the general population. Because BC reflects internal ear functioning, this not only confirms the predominance of sensorineural hearing loss but also highlights the need that special attention should be paid to these patients. In fact, the deletion of high frequencies can be disabling, leading to early communication disorders despite an overall moderate hearing loss.<sup>13</sup>

One may expect the HAART-naive patients to have better hearing than the HAART-experienced patients. However, of interest, patients receiving second-line HAART had significantly

better pure tone averages than the HAART-naive patients, who in their turn had better results than the patients receiving first-line HAART. This finding reflects the efficacy of HAART in improving immune status. In fact, the worse the immune status, the worse the hearing.<sup>22</sup> Some hearing loss may heal as patients enter second-line regimens. The healing from ARV-induced hearing loss has been described.<sup>22</sup> The second-line regimens are composed of newer and safer compounds than those used in first-line regimens. Therefore, the patients could be more observant.

Our results support the theory of the deleterious effects of HIV and HAART on hearing. However, the current study has some limitations. First, it is limited to the 15- to 49-year-old age range. The results could be different in children. However, Palacios et al<sup>29</sup> conducted a study on 23 HIV-positive children aged 5 months to 16 years receiving HAART who had alterations in PTA and brainstem-evoked response audiometry, suggesting that HIV-infected children receiving HAART are prone to hearing damage. Second, fixed-dose combination HAART renders it difficult to study the specific effect of each particular molecule because it keeps its own properties despite the synergistic association. Third, we did not have information on the observance of HAART, and we enrolled patients who had taken potentially ototoxic drugs more than 3 months before their recruitment. The effect of those drugs could be longer-lasting. However, this finding depicts the difficulty of such research in a context where traditional medicines are widely used and most of people, especially HIV patients, are reluctant to participate in research, although it is free of charge. Fourth, we did not perform high-frequency audiometry or distortion product otoacoustic emissions that could better characterize hearing changes,<sup>13,30</sup> although the use of high-frequency audiometry is still problematic in the absence of a consensus, as is the case for conventional PTA.<sup>11</sup> Fifth, we ruled out otosyphilis and cytomegalovirus infections by file and medical history check. Yet they may be of concern according to Assuiti et al.<sup>11</sup> These authors suggest that cytomegalovirus, frequent in the Brazilian population (90% of serum prevalence in São Paulo), could become activated, especially in immunocompromised patients. In Cameroon, the serum prevalence of cytomegalovirus is estimated to be almost ubiquitous in the adult population,<sup>31</sup> whereas that of syphilis is only 5.7%, as found by Noubiap et al<sup>32</sup> in a blood donor population. These pathogens may harm the ears of the HIV-positive patients, causing hearing loss by themselves or by facilitating or enhancing injury by noise and other agents.<sup>33</sup>

These results support the hypothesis that HIV-infected patients need monitoring of their hearing at all stages of the disease. Clinical and audiologic follow-up should be performed and appropriate measures taken as soon as possible when an ear symptom is reported.

---

## Conclusions

This study confirms that HIV-positive patients have poorer hearing than their HIV-negative counterparts. However, no ARV regimens could be clearly identified as harmful, and no ef-

fects of HIV were clearly isolated from those of HAART. Therefore, it is important to continue educating HIV-positive patients to react quickly to symptoms, with special attention given to hearing. Larger and more analytical studies on the effects of HIV and ARV drugs on hearing are still needed to better understand the challenges and improve care and treatment.

#### ARTICLE INFORMATION

**Submitted for Publication:** August 5, 2014; final revision received November 16, 2014; accepted December 10, 2014.

**Published Online:** March 5, 2015.  
doi:10.1001/jamaoto.2015.125.

**Author Affiliations:** Department of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon (Fokouo, Vokwely, Bengono, Njock); National Social Insurance Fund Hospital, Yaoundé, Cameroon (Vokwely); Edéa Regional Hospital, Edéa, Cameroon (Noubiap, Njock); Medical Diagnostic Center, Yaoundé, Cameroon (Noubiap); Department of Internal Medicine, University of British Columbia, Vancouver, British Columbia, Canada (Nouthe); Department of Preventive and Social Medicine, Laval University, Québec City, Québec, Canada (Zafack); Douala General Hospital, Douala, Cameroon (Minka Ngom, Njock); Yaoundé General Hospital, Yaoundé, Cameroon (Dalil); Geneva Teaching Hospital, Geneva, Switzerland (Ngo Nyeki).

**Author Contributions:** Drs Fokouo and Vokwely had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Fokouo, Vokwely, Ngom, Njock.

**Acquisition, analysis, or interpretation of data:** Fokouo, Noubiap, Nouthe, Zafack, Asmaou, Nyeki, Bengono.

**Drafting of the manuscript:** Fokouo, Noubiap, Nouthe. **Critical revision of the manuscript for important intellectual content:** Vokwely, Noubiap, Zafack, Ngom, Asmaou, Nyeki, Bengono, Njock.

**Statistical analysis:** Noubiap, Nouthe, Zafack. **Obtained funding:** Fokouo.

**Administrative, technical, or material support:** Fokouo, Vokwely, Ngom, Asmaou, Nyeki.

**Study supervision:** Bengono, Njock.

**Conflict of Interest Disclosures:** None reported.

**Additional Contributions:** We thank Gisele Alenda, MD, for revising the English, the patients who participated in the study, and the authorities and staff of the National Social Insurance Fund Hospital for their collaboration, commitment, and availability.

#### REFERENCES

- UNAIDS. *The Gap Report*. Geneva, Switzerland: UNAIDS; 2014.
- Prasad HK, Bhojwani KM, Shenoy V, Prasad SC. HIV manifestations in otolaryngology. *Am J Otolaryngol*. 2006;27(3):179-185.
- Lubbe D. HIV and ENT. *Contin Med Educ*. 2004;22(5):250-253.
- Ondzotto G, Ibara JR, Mowondabeka P, Galiba J. Cervico-facial and ENT symptoms due to HIV infection in a tropical area: about 253 Congolese cases [in French]. *Bull Soc Pathol Exot*. 2004;97(1):59-63.
- Mata Castro N, Yebra Bango M, Tutor de Ureta P, Villarreal García-Lomas M, García López F. Hearing loss and human immunodeficiency virus infection: study of 30 patients [in Spanish]. *Rev Clin Esp*. 2000;200(5):271-274.
- Matas CG, Santos Filha VA, Juan KR, Pinto FR, Gonçalves IC. Audiological manifestations in children and adults with AIDS. *Pro Fono*. 2010;22(3):269-274.
- Khoza K, Ross E. Auditory function in a group of adults infected with HIV/AIDS in Gauteng, South Africa. *S Afr J Commun Disord*. 2002;49:17-27.
- Wang Y, Yang H, Dong M. The hearing manifestations of 350 patients of AIDS [in Chinese]. *Lin Chuang Er Bi Yan Hou Ke Za Zhi*. 2006;20(22):1020-1021.
- Zuniga J. Communication disorders and HIV disease. *J Int Assoc Physicians AIDS Care*. 1999;5(4):16-23.
- Comité National de Lutte contre le Sida. *L'impact du VIH et du SIDA au Cameroun à l'horizon 2020*. Yaoundé, Cameroon: Comité National de Lutte contre le Sida; 2010.
- Assuiti L, Lanzoni GdM, Santos Fd, Erdmann AdL, Meirelles B. Perda auditiva em pessoas com HIV/AIDS e fatores relacionados: uma revisão integrativa. *Braz J Otorrinolaryngol*. 2013;79(2):248-255.
- Mrema Y. *Critical Review: What Is the Existing Evidence of the Impact of Antiretroviral Drugs and Human Immunodeficiency Virus on the Auditory System?* London, England: University of Western Ontario; 2008.
- Khoza-Shangase K. Is there a need for ototoxicity monitoring in patients with HIV/AIDS? *Afr J Pharm Pharmacol*. 2010;4(9):574-579.
- Khoza-Shangase K. An analysis of auditory manifestations in a group of adults with AIDS prior to antiretroviral therapy. *Afr J Infect Dis*. 2011;5(1):11-22.
- Comité National de Lutte contre le Sida. *Fiche Présentation Étude de l'Impact du VIH au Cameroun Août 2010*. Yaoundé, Cameroon: Comité National de Lutte contre le Sida; 2010.
- CAMEROUN: 33 000 morts du Sida en 2010! <http://koaci.com/articles-71699>. Accessed February 11, 2012.
- Bengono G, Binam F, Ndjolo A, Essame Oyono J, Fouda Onana A, Djeugabeng F. La pathologie ORL et l'infection au VIH à Yaoundé. *Bull Liais Doc OCEAC*. 1999;32(3):15-19.
- Ndjolo A, Njock R, Ngowe NM, et al. Manifestations Oto-Rhino-Laryngologiques inaugurales de l'infection à VIH/SIDA: analyse de 76 cas observés en milieu africain. *Rev Laryngol Otol Rhinol (Bord)*. 2004;125(1):39-43.
- Bureau International d'Audio-Phonologie. *Classification Audiométrique des Déficiences Auditives (recommandation BIAP O2/1 bis)*. 2013. <http://www.biap.org/fr/recommandations/65-ct-2-classification-des-surdites/5-recommandation-biap-O2-1-bis>. Accessed February 9, 2013.
- World Health Organization. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach*. Geneva, Switzerland: World Health Organization; 2013.
- Chandrasekhar SS, Connelly PE, Brahmabhatt SS, Shah CS, Kloser PC, Baredes S. Otologic and audiologic evaluation of human immunodeficiency virus-infected patients. *Am J Otolaryngol*. 2000;21(1):1-9.
- Marra CM, Wechkin HA, Longstreth WT Jr, Rees TS, Syapin CL, Gates GA. Hearing loss and antiretroviral therapy in patients infected with HIV-1. *Arch Neurol*. 1997;54(4):407-410.
- Soumaré M, Seydi M, Ndour CT, et al. Epidemiological, clinical etiological features of neuromeningeal diseases at the Fann Hospital Infectious Diseases Clinic, Dakar (Senegal) [in French]. *Med Mal Infect*. 2005;35(7-8):383-389.
- Domènech J, Fusté J, Traserra J. Equilibrium and auditory disorders in patients infected by HIV-1 [in French]. *Rev Neurol*. 1996;24(136):1623-1626.
- van der Westhuizen Y, Swanepoel W, Heinze B, Hofmeyr LM. Auditory and otological manifestations in adults with HIV/AIDS. *Int J Audiol*. 2013;52(1):37-43.
- Grimaldi LM, Luzi L, Martino GV, et al. Bilateral eighth cranial nerve neuropathy in human immunodeficiency virus infection. *J Neurol*. 1993;240(6):363-366.
- Brette M, Ben Bahmed R, Monteil J. Manifestations oto-rhino-laryngologiques et séropositivité au virus de l'immunodéficience humaine. In: *Encyclopédie Médico-Chirurgicale*. Paris, France: EMC Publishing; 2007:20-956-A-910.
- Obasikene G, Adobamen P, Okundia P, Ogusi FO. Prevalence of ototoxicity in University of Benin Teaching Hospital, Benin City: a 5-year review. *Niger J Clin Pract*. 2012;15(4):453-457.
- Palacios GC, Montalvo MS, Fraire MI, Leon E, Alvarez MT, Solorzano F. Audiologic and vestibular findings in a sample of human immunodeficiency virus type-1-infected Mexican children under highly active antiretroviral therapy. *Int J Pediatr Otorhinolaryngol*. 2008;72(11):1671-1681.
- Campbell K. *Pharmacology and Ototoxicity for Audiologists*. Ann Arbor: Thomson Delmar Learning, University of Michigan; 2007.
- Stroffolini T, Ngatchu T, Chiaramonte M, et al. Prevalence of cytomegalovirus seropositivity in an urban childhood population in Cameroon. *New Microbiol*. 1993;16(1):83-85.
- Noubiap JJ, Joko WY, Nansseu JR, Tene UG, Siaka C. Sero-epidemiology of human immunodeficiency virus, hepatitis B and C viruses, and syphilis infections among first-time blood donors in Edéa, Cameroon. *Int J Infect Dis*. 2013;17(10):e832-e837.
- Bektas D, Martin GK, Stagner BB, Lonsbury-Martin BL. Noise-induced hearing loss in mice treated with antiretroviral drugs. *Hear Res*. 2008;239(1-2):69-78.