

Audiological manifestations in HIV-positive adults

Carla Gentile Matas,¹ Rosanna Giaffredo Angrisani,¹ Fernanda Cristina Leite Magliaro,¹ Aluisio Augusto Cotrim Segurado^{II}

^IFaculdade de Medicina da Universidade de São Paulo, Departamento de Fisioterapia, Fonoaudiologia e Terapia Ocupacional, São Paulo/SP, Brazil.

^{II}Faculdade de Medicina da Universidade de São Paulo, Departamento de Moléstias Infecciosas e Parasitárias, São Paulo/SP, Brazil.

OBJECTIVE: To characterize the findings of behavioral hearing assessment in HIV-positive individuals who received and did not receive antiretroviral treatment.

METHODS: This research was a cross-sectional study. The participants were 45 HIV-positive individuals (18 not exposed and 27 exposed to antiretroviral treatment) and 30 control-group individuals. All subjects completed an audiological evaluation through pure-tone audiometry, speech audiometry, and high-frequency audiometry.

RESULTS: The hearing thresholds obtained by pure-tone audiometry were different between groups. The group that had received antiretroviral treatment had higher thresholds for the frequencies ranging from 250 to 3000 Hz compared with the control group and the group not exposed to treatment. In the range of frequencies from 4000 through 8000 Hz, the HIV-positive groups presented with higher thresholds than did the control group. The hearing thresholds determined by high-frequency audiometry were different between groups, with higher thresholds in the HIV-positive groups.

CONCLUSION: HIV-positive individuals presented poorer results in pure-tone and high-frequency audiometry, suggesting impairment of the peripheral auditory pathway. Individuals who received antiretroviral treatment presented poorer results on both tests compared with individuals not exposed to antiretroviral treatment.

KEYWORDS: Audiometry; High-frequency Hearing Loss; Acquired Immunodeficiency Syndrome; HIV.

Matas CG, Angrisani RG, Magliaro FC, Segurado AA. Audiological manifestations in HIV-positive adults. *Clinics*. 2014;69(7):469-475.

Received for publication on December 19, 2013; First review completed on January 9, 2014; Accepted for publication on January 9, 2014

Corresponding author Email: cgmatas@usp.br

Tel.: 55 11 3091-8411

■ INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is caused by human immunodeficiency virus (HIV), the etiological agent that causes significant immunological impairment in individuals with AIDS. This retrovirus mainly invades cells related to the immune system, triggering a progressive reduction of lymphocyte and hence causing opportunistic infections. HIV is transmitted by sexual intercourse, blood transfusion, the use of injection drugs, occupational accidents and perinatal transmission (1). In Brazil, HIV prevalence is approximately 0.6% in the population between 15 and 49 years of age, 0.4% among women and 0.8% among men (2).

Nearly 75% of adults with AIDS present some types of hearing impairment due to opportunistic infections or treatments with ototoxic medications (3). The incidence of

hearing impairment among patients with HIV/AIDS varies from 20% to 40% (4-7) and the hearing loss may be due to outer, middle and/or inner ear pathologies.

Infections of the upper airways, and especially sinusitis, external otitis, and otitis media, are among the infections that might affect individuals with AIDS (8). It is known that otitis media may cause temporary peripheral hearing loss and must be diagnosed as early as possible so that adequate medical treatment is established. These individuals may also present cochlear pathology/inner ear impairments due to the direct action of the virus (5,6,9,10) and the use of antiretroviral drugs and/or potentially ototoxic medications (11), which can cause sensorineural hearing loss.

This is the first study in a series of two that intended to examine the audiological manifestations of HIV's action on the auditory system, from its most peripheral to its most central portion, in seropositive individuals. The aim of this first study was to characterize the audiological profile of HIV-positive individuals and to compare the results obtained between HIV-positive individuals who received and did not receive antiretroviral treatment (ART).

■ MATERIALS AND METHODS

The present research consisted of a prospective cross-sectional study that was approved by the Ethics Committee

Copyright © 2014 **CLINICS** – This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

No potential conflict of interest was reported.

DOI: 10.6061/clinics/2014(07)05



for the Analysis of Research Projects (CAPPesq) of the Clinical Board of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP), under protocol number 1026/04.

All participants signed the Free and Informed Consent Term, according to Resolution 196/96. The procedures were conducted at the Investigation Laboratory in Auditory Evoked Potentials of the Department of Physical Therapy, Speech-Language Pathology and Audiology and Occupational Therapy of the Faculdade de Medicina da Universidade de São Paulo (FMUSP).

The participants were 75 individuals aged from 20 to 60 who were divided into three groups (see the descriptions of the groups in Table 1):

Research Group I (RGI): composed by 18 HIV-positive subjects (confirmed by serology) not exposed to ART.

Research Group II (RGII): composed by 27 HIV-positive subjects (confirmed by serology) exposed to ART with at least three of the following drugs (combination therapy or highly active antiretroviral therapy): lamivudine, zidovudine, efavirenz, didanosine, nevirapine, lopinavir-r, tenofovir, stavudine, indinavir, abacavir, amprenavir, ritonavir, and atazanavir.

Control Group (CG): composed by 30 non-HIV-infected subjects (confirmed by serology) with no medical history of psychiatric or neurological conditions and no audiological or auditory processing complaints.

For all three groups, the following exclusion criteria were considered: pregnancy, ongoing opportunistic infections, the presence of any other clinical and/or cognitive impairment that could prevent the adequate conduction of audiological exams and a history of otologic surgery and/or otologic diseases not related to HIV.

RGI and RGII were referred by Casa da AIDS – Fundação Zerbini and by the Health Services of the Municipal Network Specializing in Sexually Transmitted Diseases (STD/AIDS) of the São Paulo Department of Health.

Data regarding eligibility criteria of the sample, as well as the presence of risk indicators for hearing impairments reported in the case history were retrieved from subjects' records. Auditory complaints were obtained through a closed-ended questionnaire. Subsequently, a visual inspection of the external ear canal was performed using a Heine otoscope.

Acoustic immittance measures (tympanometry and ipsilateral and contralateral acoustic reflex measures for frequencies of 500, 1000, 2000 and 4000 Hz) were performed

Table 1 - Descriptive analysis of the Control Group, Research Group I, and Research Group II regarding gender, age, hearing complaints, CD4+ T lymphocytes and the duration of HIV infection.

	CG	RGI	RGII
Number of subjects	30	18	27
♀:♂	14:16	4:14	9:18
Age*	25.6 ± 6.1	39.4 ± 8.1	40.3 ± 6.7
Hearing complaints (%)	-	61	89
CD4+**	-	585.3 ± 242.0	477.0 ± 273.3
Duration of infection***	-	86.5 ± 57.7	111.6 ± 57.5

♀: female; ♂: male.

*In years (mean ± standard deviation).

**Cells per mm³.

***In months.

for the electroacoustic assessment of hearing using the middle ear analyzer model GSI-33 from Grason Stadler (ANSI S3.39-1987). Each subject was instructed to remain quiet, to refrain from talking, and to minimize head movement. The results were classified as normal or altered according to the normality criteria described: a type A tympanometric curve; ipsilateral acoustic reflexes present at frequencies of 500, 1000 and 2000 Hz between 80 and 95 dB HL; and contralateral acoustic reflexes present at frequencies of 500, 1000 and 2000 Hz between 90 and 105 dB HL (12,13).

The behavioral hearing assessment (conventional pure-tone audiometry (PTA) and high-frequency audiometry (HFA)) was conducted using the audiometer model GSI-61 from Grason Stadler. Model TDH-50 supra-aural headphone (Telephonics) was used for conventional PTA, and for HFA, model HDA-200 (Sennheiser) (standards ANSI S3.6-1989 and IEC-1988) was used. The subject had to remain seated in a soundproof booth (ANSI S3.1-1991 standard of environmental quantity of noise).

All individuals were initially tested by PTA at frequencies of 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 Hz, and, when necessary, bone-conduction testing was performed at frequencies of 500, 1000, 2000, 3000 and 4000 Hz. Speech audiometry, consisting of speech recognition threshold (SRT) testing and suprathreshold word-recognition testing (SWRT), used the lists of words proposed by Santos and Russo (14).

The PTA results were classified as normal or abnormal, with the following considered as normal: hearing thresholds lower than or equal to 20 dB HL for the frequencies tested (15); SRT responses up to or equal to 10 dB over the hearing thresholds obtained at frequencies of 500, 1000 and 2000 Hz during the PTA (14); and SWRT with a percentage of correct answers between 88% and 100% at an intensity 30 dB above the SRT (16). Abnormal results in the PTA were classified as follows: high-frequency sensorineural hearing loss (altered results over 3000 Hz), conductive hearing loss, mixed hearing loss, sensorineural hearing loss and conductive hearing loss or mixed hearing loss plus sensorineural hearing loss (when each ear presented a different result) (17).

The HFA was also conducted through air conduction at frequencies of 9000, 10000, 11200, 12500, 14000, 16000, 18000 and 20000 Hz. According to a study by Burguetti et al. (18) and considering that HFA is performed in 5-dB HL intervals, the following cutoff values were established as normal, based on frequency and age range (Table 2):

Both electroacoustic and behavioral assessments were performed by the same evaluator (a certified audiologist) and on the same day to avoid the effects of other variables on the results.

When abnormal results were obtained, the patient was referred for otorhinolaryngological assessment and treatment

Table 2 - Normality cutoff values in high-frequency audiometry (in dB HL) by frequency and age range.

	9 kHz	10 kHz	12.5 Hz	14 kHz	16 kHz	18 kHz	20 kHz
20-29 years	15	15	15	15	30	30	10
30-39 years	30	30	35	45	55	35	15
>40 years	30	35	55	90	60	40	20



and instructed to return in three months for audiological monitoring.

Statistical methods

The electroacoustic and behavioral results were qualitatively and quantitatively analyzed for all three groups.

In the analysis of qualitative data (categorical), the results were described as proportions of alterations and as types of alterations according to the assessment criteria. For this purpose, the Chi-squared test (X^2) (without Yates correction) was used, following the Cochran restrictions; when these restrictions were present, Fisher’s exact test was performed.

For the analysis of quantitative (continuous) data, the mean, median, standard deviation, minimum and maximum values were obtained for the results of each assessment in each group. Additionally, the mean values obtained for RGI, RGII and the CG were compared, and the significance level was verified for each comparison. This analysis applied the Mann-Whitney U test in the case of two independent samples or the Kruskal-Wallis test in the case of three or more independent samples and the Wilcoxon signed rank test (Z). Differences between means were tested using one-way analysis of variance (ANOVA) (F) in the case of three or more samples.

The Spearman correlation coefficient (r) was used to evaluate the relationship between continuous variables and the biserial correlation coefficient (rb) was used to evaluate the relationship between categorical and continuous variables. Lacking data were excluded from the analysis.

Probability values (p) lower than 0.05 were considered statistically significant, except when a potential problem involving multiple comparisons was identified. In this case, the Bonferroni correction (calculated by dividing 0.05 by the number of multiple comparisons performed) was used. This situation occurred in the following analyses: the comparison between right and left ear scores and the comparison of the hearing assessment parameters between groups (corrected p-value of 0.001).

In the qualitative analyses, when the proportions of alterations in behavioral and electroacoustic assessments were compared, the corrected p-value was 0.005 because nine analyses were performed. When two-by-two analyses were conducted, the corrected p-value was 0.017 (three analyses).

All analyses used Statistical Package for the Social Sciences (SPSS) 15 for Windows.

RESULTS

Data regarding the auditory complaints reported in the questionnaire revealed no significant differences between RGI and RGII ($p=0.064$): 61% of RGI and 89% of RGII presented hearing complaints. The most frequent symptom found among HIV-positive subjects in RGI was dizziness (61% of the cases), followed by tinnitus (39%) and a sensation of ear fullness (33%). In RGII, hearing loss was most frequent (52% of the cases), followed by tinnitus (44%) and dizziness (33%).

The comparison between the right and left ears for each group (Wilcoxon signed rank test) did not show significant differences for any frequencies in the PTA and also for the SRT and SWRT. Hence, the three groups were compared based on the mean values for the right and left ears of each subject (Figure 1).

The results obtained in the PTA, SRT and SWRT were significantly different between the CG, RGI and RGII (Kruskal-Wallis test, $p<0.001$). To identify where these differences occurred, the Mann-Whitney test was used to compare the groups in pairs and the Bonferroni correction was used in sequence for multiple comparisons (a significance level of $p<0.017$ was used in this test).

This group comparison evidenced the following results: the mean hearing thresholds obtained in the PTA from 250 to 2000 Hz and in the SRT of RGII were significantly higher than in the other groups ($p<0.001$). At a frequency of 3000 Hz in the PTA, the mean hearing thresholds in the CG were significantly lower than in RGI ($p<0.004$), which were lower than in RGII ($p<0.003$). The mean hearing thresholds obtained in the PTA from 4000 to 8000 Hz were significantly lower in the CG than in the other groups ($p<0.001$). The mean results in the SWRT were higher in RGII than in the CG ($p<0.001$).

No significant differences were evident between the hearing thresholds obtained in the HFA for the right and left ears for all groups (Wilcoxon signed-rank test). Thus, for the subsequent analyses, the mean values for both ears were used.

The comparative analysis of the hearing thresholds obtained in the HFA (Figure 2) showed significantly

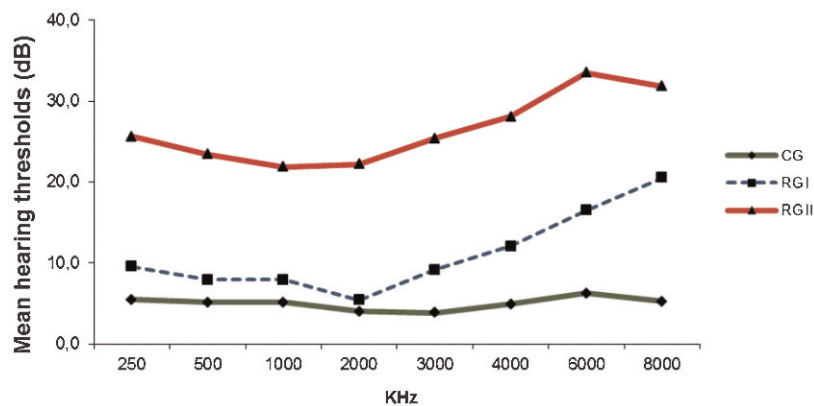


Figure 1 - Mean hearing thresholds for the pure-tone audiometry frequencies in both the right and the left ears for the Control Group, Research Group I, and Research Group II.

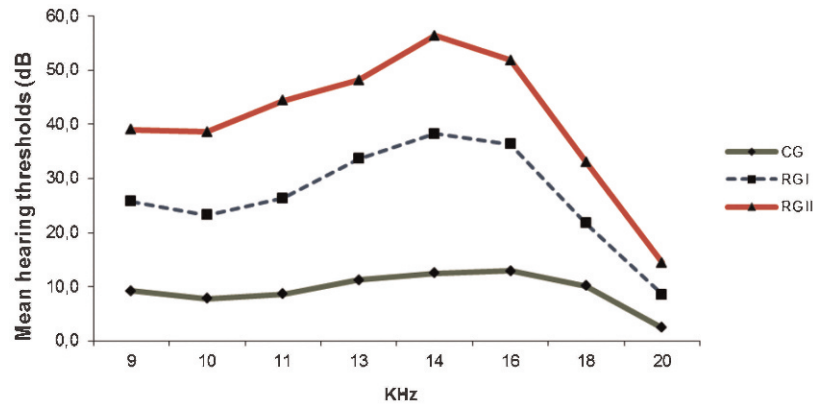


Figure 2 - Mean hearing thresholds for the high-frequency audiometry frequencies in both the right and left ears for the Control Group, Research Group I, and Research Group II.

different values between the CG, RGI and RGII at all frequencies assessed (Kruskal-Wallis test, $p < 0.001$).

The Mann-Whitney test was used for two-by-two comparisons, followed by the Bonferroni correction for multiple comparisons (with a significance level of $p < 0.017$), to identify where these differences occurred. These analyses showed that the mean hearing thresholds obtained in the CG at all high frequencies (except 10 kHz, for which $p = 0.033$) were significantly lower than those obtained in RGI. The two-by-two comparisons between the CG and RGII yielded significant results ($p < 0.001$) for all high frequencies. In contrast, the comparisons between RGI and RGII did not show significant differences (Table 3).

It is important to emphasize the significant differences obtained between the proportions of alterations in the HFA and in the PTA for all three groups in the present study. Considering the three groups, there was a higher proportion of alterations in the HFA compared with the PTA. RGI presented 27.8% of alterations in the PTA and 58.8% in the HFA, and RGII presented 48.1% of the altered results in the PTA and 73.9% in the HFA (4).

Regarding the proportions of the types of hearing alterations in the PTA, 80% of high-frequency sensorineural hearing loss and 20% of conductive hearing loss occurred in RGI, whereas RGII presented 38.5% of sensorineural hearing loss, 30.8% of conductive hearing loss and 15.4% of high-frequency sensorineural hearing loss (Table 5).

DISCUSSION

In the present study, individuals in both RGI (not exposed to ART) and RGII (exposed to ART) presented with auditory complaints. Many studies in the literature have reported an association between HIV infection and otoneurological signs and symptoms, emphasizing that subjects with AIDS frequently present with auditory complaints due to otorhinolaryngological/otologic manifestations that are common in any stage of the disease and that cause specific symptoms, such as hearing loss, tinnitus, dizziness, and sensations of ear fullness (4-7,19-24).

In a study by Ceccarelli et al. (20), the most frequent auditory complaints among AIDS patients in the initial or asymptomatic stage were tinnitus (in 50% of the cases) and vertigo (35%). Subjects also complained of hearing loss (25% of the cases), a sensation of ear fullness (15%), non-rotatory dizziness (10%) and unspecific headache (20%). In the

present study, the most frequent symptom reported by seropositive individuals not exposed to ART (RGI) was dizziness (61% of the cases) and in the group exposed to ART (RGII), hearing loss was most frequent (52% of the cases). These results are in agreement with the symptoms reported in the previous study, although with different proportions.

Table 3 - Two-to-two comparisons of the Control Group, Research Group I, and Research Group II regarding the hearing thresholds obtained at high frequencies according to the Mann-Whitney test.

Comparison between groups	U	Z	p
9 kHz			
CG X RGI	130.00	-2.79	0.005*
CG X RGII	84.00	-4.71	<0.001*
RGI X RGII	137.50	-1.59	0.111
10 kHz			
CG X RGI	159.50	-2.13	0.033
CG X RGII	74.50	-4.88	<0.001*
RGI X RGII	131.50	-1.76	0.079
11.2 kHz			
CG X RGI	125.50	-2.88	0.004*
CG X RGII	41.00	-5.47	<0.001*
RGI X RGII	117.00	-2.15	0.032
12.5 kHz			
CG X RGI	133.50	-2.70	0.007*
CG X RGII	59.00	-5.14	<0.001*
RGI X RGII	145.50	-1.37	0.171
14 kHz			
CG X RGI	123.50	-2.93	0.003*
CG X RGII	33.00	-5.61	<0.001*
RGI X RGII	123.00	-1.99	0.047
16 kHz			
CG X RGI	111.00	-3.20	0.001*
CG X RGII	19.00	-5.86	<0.001*
RGI X RGII	116.50	-2.17	0.030
18 kHz			
CG X RGI	112.00	-3.18	0.001*
CG X RGII	12.50	-5.99	<0.001*
RGI X RGII	82.00	-3.13	0.002
20 kHz			
CG X RGI	107.00	-3.13	0.002*
CG X RGII	31.00	-5.70	<0.001*
RGI X RGII	96.00	-2.56	0.010

$p < 0.017$ was considered to indicate statistical significance according to the Bonferroni correction.



Another study observed that 8.6% of 162 patients treated with antiretroviral drugs and 5.8% of 122 untreated patients reported otoneurological complaints (23). Hearing loss, accompanied or unaccompanied by tinnitus, represented 78.5% of the complaints in the treated group and 57.1% in the untreated group. These findings were not corroborated by the present study, in which both individuals exposed (RGII) and individuals not exposed (RGI) to ART predominantly presented hearing complaints (89% and 61%, respectively).

The results obtained in the PTA at all frequencies tested, as well as in the SWRT, were different between groups. RGII presented higher hearing thresholds than CG at all frequencies and than RGI at frequencies from 250 to 3000 Hz. Significant differences between groups were also found in the comparison of the proportions of alterations in the PTA: RGI and RGII had higher proportions of hearing loss compared with the CG (27.8% and 48.1%, respectively). These results corroborate the data presented by Salzer (19) and Carvalho et al. (25), who referred to hearing loss as a common otologic manifestation in HIV-positive individuals, and the findings of many other authors who verified that hearing alterations can be present in up to 33% of HIV-positive patients (4-7,26).

However, the results obtained disagree with those found in a study with 30 seropositive patients, which reported normal results for conventional PTA (27).

Many hypotheses can be posited about the causes of the auditory manifestations observed in the HIV-positive groups in this study. Regarding RGI, the hearing loss might have been due to the direct action of the virus on the auditory system structures (23,28,29). As for RGII, the possible etiological factors associated with the hearing loss might have been the direct action of the virus on the auditory system structures, the presence of opportunistic infections and/or the use of ototoxic drugs (25,30).

RGII was more susceptible to auditory alterations compared with RGI. A possible interpretation of these data is that the use of antiretroviral drugs may have caused a higher incidence of hearing loss due to its ototoxicity, especially with the new antiretroviral therapies currently used (combined therapy or highly active antiretroviral therapy (HAART)). This aspect has been emphasized in the literature by many researchers (22,29,30).

In the study with HIV-positive patients, the group submitted to antiretroviral therapy presented higher susceptibility to hearing loss than untreated individuals, which was evidenced by a higher occurrence of hearing alterations in the individuals exposed to antiretroviral therapy (29).

It is worth emphasizing that all RGII patients in the present study used combined therapy (HAART), which has been reported in the literature as the cause of adverse side effects, such as ototoxicity (22,31-33). However, this aspect was not observed in a study that assessed two groups of patients (exposed or not exposed to antiretroviral drugs) and did not find a significant correlation between antiretroviral therapy and ototoxicity (23).

Another hypothesis is that because RGII was composed of individuals with a longer duration of HIV infection (mean of 111.6 months), these subjects may have been exposed to the direct action of the virus on the auditory system structures for longer. These aspects have also been mentioned in specialized literature (30).

The diversity of auditory alterations observed in HIV-positive patients in the present study was also described by a previous study, which indicated that these subjects' hearing loss could be either conductive or sensorineural, in varied degrees (from mild to profound) and with no specific configuration (6).

Regarding the types of alterations found in the PTA in the present study, the most frequently observed alteration in both HIV-positive groups was sensorineural hearing loss: in RGI, high-frequency sensorineural hearing loss (80% of altered cases were at frequencies over 3000 Hz) and in RGII, sensorineural hearing loss also affecting middle and low frequencies (38.5% of the altered cases). These findings corroborate those reported in the literature (5,30,34-36), which found a predominance of sensorineural hearing loss in HIV-positive patients, mainly at high frequencies.

Regarding inner ear alterations, sensorineural hearing loss in individuals with HIV may be due to opportunistic diseases or ototoxic drugs (32). These authors attributed the hearing loss associated with antiretroviral therapy to mitochondrial DNA lesions.

According to several studies, sensorineural hearing loss in individuals with HIV/AIDS has typically been observed to undergo a steeper decrease at high frequencies, similar to the results for RGI in the present study (5,30,34). Considering this type of audiometric configuration, a significant difference was found between RGI and RGII (80% of occurrences in RGI and 15.4% in RGII).

In compiling the international literature, it is estimated that 20% to 50% of the HIV-positive population presents different levels of sensorineural hearing loss. Several authors have noted that sensorineural hearing loss appears to be less severe in patients with more serious HIV infections (4,5). This phenomenon explains why, in the present study, RGI presented sensorineural hearing loss only at higher frequencies, whereas RGII experienced sensorineural loss that also affected hearing at middle and low frequencies.

The second most frequent alteration found in the PTA for RGI and RGII was conductive hearing loss due to middle-ear impairments, which was present in 20% of the altered cases in RGI and in 30.8% in RGII. Hence, as in other studies (4,19,37), we verified the presence of conductive and/or sensorineural hearing loss in HIV-infected individuals.

Regarding conductive impairments, both groups (RGI and RGII) presented conductive or mixed hearing loss, which was observed in 15.4% of the altered cases in RGII. Authors have reported the occurrence of otorhinolaryngological manifestations in patients with HIV (37) and have verified that 20% of the subjects evaluated presented otologic complaints. Additionally, chronic otitis media was the otologic disease most commonly found.

We emphasize that the RGII presented higher proportion of conductive hearing loss than RGI, which may be due to the fact that the RGII is composed by individuals infected by HIV for a longer time and, hence, presenting steeper immunosuppression, resulting in higher vulnerability to infections, like otitis media.

Regarding the HFA, the hearing thresholds obtained at all frequencies tested were significantly different between groups, and RGI and RGII presented higher thresholds for the frequencies between 9 kHz and 20 kHz compared to CG.



Table 4 - Comparisons of proportions of alterations in the behavioral and electroacoustic assessments of hearing between the Control Group, Research Group I and Research Group II (Chi-squared test or Fisher's exact test).

Assessment	CG	RGI	RGII	X ²	p
Behavioral					
PTA	0.0%	27.8%	48.1%	-	<0.001*
HFA	16.7%	58.8%	73.9%	18.73	<0.001*
Speech audiometry (SRT, SWRT)	0.0%	0.0%	26.9%	-	0.001*
Electroacoustic					
Acoustic immittance measures	13.3%	33.3%	40.7%	5.63	0.078

Significance level: $p < 0.005$, Bonferroni correction.

PTA: pure-tone audiometry; HFA: high-frequency audiometry; SRT: speech recognition threshold; SWRT: suprathreshold word-recognition testing.

These results corroborate the findings of Juan (35), who observed significant differences in the hearing thresholds presented by subjects with HIV/AIDS and healthy individuals during HFA at all frequencies tested; the thresholds were higher among the individuals with HIV/AIDS.

In the comparison between groups regarding the proportions of alterations in the HFA, significant differences were verified (Table 4), with a higher proportion of alterations in RGI and RGII (58.8% and 73.9%, respectively) than in the CG (16.7%). A higher incidence of HFA alterations in HIV-positive individuals was also found in studies reported in the specialized literature (27,29,35). Whereas Domenech et al. (27) observed the presence of alterations in the HFA of 23% of the seropositive patients in their sample, Juan (35) verified that 88% of individuals with HIV/AIDS had HFA alterations.

However, in the present study, no significant difference was found between RGI and RGII regarding the proportions of alterations in the HFA. It was verified that the group exposed to ART presented with a higher percentage of altered results (73.9%) than the group not exposed to treatment did (58.8%). These results corroborate those of Matas et al. (29), who also found more HFA alterations in a group exposed to ART compared with a group that was not exposed.

The great difference obtained between the proportions of alterations in the HFA and in PTA for all three groups emphasizes the importance of conducting HFA in HIV-positive patients, since this assessment was sensitive to early identify hearing impairments that would not be detected in conventional PTA. As in the PTA, these high-frequency hearing impairments might be due to the use of potentially ototoxic medications, as noted by several previous studies that researched the ototoxicity of antiretroviral therapy, especially given the association with different drugs (22,31,38). Alternatively, the hearing loss at high frequencies may be caused by the direct action of the

Table 5 - Proportions of types of hearing loss in Research Groups I and II.

PTA	RGI (%)	RGII (%)
CHL/MHL+SNHL	0.0	15.4
CHL	20.0	30.8
SNHL	0.0	38.5
HFSNHL	80.0	15.4
Total	100.0	100.0

PTA: pure-tone audiometry, CHL: conductive hearing loss; MHL: mixed hearing loss; SNHL: sensorineural hearing loss; HFSNHL: high-frequency sensorineural hearing loss.

virus on the inner ear structures with the progression of the disease (4,30,39).

Otorhinolaryngological manifestations are common in individuals with AIDS (21). Thus, we emphasize the importance of early diagnosis and of aggressive treatment for otologic diseases related to HIV, with the aim of providing significant improvement of the symptoms.

HIV-positive individuals present alterations in behavioral and electroacoustic assessments of hearing (PTA, HFA, and acoustic immittance measures), suggesting impairment in the peripheral auditory pathway. The group exposed to ART presents higher proportion of alterations than the group not exposed to this treatment.

ACKNOWLEDGMENTS

We thank the São Paulo Research Foundation (FAPESP – *Fundação de Amparo à Pesquisa do Estado de São Paulo*) for the grants for this study.

AUTHOR CONTRIBUTIONS

Matas CG, Angrisani RG, Magliaro FC and Segurado AA conceived and designed the study, were responsible for data analysis and interpretation, critically revision of the manuscript for important intellectual content, manuscript draft and approval of the final version to be published. Matas CG and Magliaro FC were responsible for data acquisition.

REFERENCES

- Friedland GH, Klein RS. Transmission of the human immunodeficiency virus. *N Engl J Med.* 1987;317(18):1125-35.
- Brasil. Ministério da Saúde. Coordenação Nacional DST/AIDS. Boletim epidemiológico – AIDS. Brasília: Centro de Documentação do Ministério da Saúde. 2010;Ano VI,nº. 1.
- Zuniga J. Communication Disorders and HIV disease. *J IntAssoc Physicians AIDS Care.* 1999;5(4):16-23.
- 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.
- Mata Castro N, Yebra Bango M, Tutor de Ureta P, Villarreal Garcia-Lomas M, Garcia Lopez F. Hearing loss and human immunodeficiency virus infection. Study of 30 patients. *Rev Clin Esp.* 2000;200(5):271-4.
- Khoza K, Ross E. Auditory function in a group of adults infected with HIV/AIDS in Gauteng, South Africa. *S Afr J CommunDisord.* 2002;49:17-27.
- Van der Westhuizen Y, Swanepoel de W, Heinze B, Hofmeyr LM. Auditory and ontological manifestations in adults with HIV/AIDS. *Int J Audiol.* 2013;52(1):37-43.
- Matkin ND, Diefendorf AO, Erenberg A. Children: HIV/AIDS and hearing loss. *Seminars in Hearing.* 1998;19(2):143-53, <http://dx.doi.org/10.1055/s-0028-1082964>.
- Chandrasekhar SS, Siverls V, Sekhar HKC. Histopathologic and ultrastructural changes in the temporal bones of HIV-infected human adults. *Am J Otol.* 1992;13(3):207-14.



10. Pappas DG Jr, Roland JT Jr, Lim J, Lai A, Hillman DE. Ultrastructural findings in the vestibular end-organs of AIDS cases. *Am J Otol.* 1995;16(2):140-5.
11. Reyes-Contreras L, Silva-Rojas A, Ysunza-Rivera A, Jimenez-Ruiz G, Berruecos-Villalobos P, Romo-Gutierrez G. Brainstem auditory evoked response in HIV – infected patients with and without AIDS. *Arch Med Res.* 2002;33(1):25-8, [http://dx.doi.org/10.1016/S0188-4409\(01\)00342-3](http://dx.doi.org/10.1016/S0188-4409(01)00342-3).
12. Jerger J. Clinical experience with impedance audiometry. *Arch Otolaryngol.* 1970;92(4):311-24, <http://dx.doi.org/10.1001/archotol.1970.04310040005002>.
13. Carvalho RMM, Carvalho M, Ishida IM. Auditory profile in individuals with and without CAPD. In: 12th Annual Convention & Exposition of the American Academy of Audiology. Chicago. USA. 2000:195.
14. Santos TMM, Russo ICP. Logaudiometria. In: Santos TMM, Russo ICP. *A prática da audiologia clínica.* Cortez. 2ª edição. São Paulo. 1991:73-88.
15. British Society of Audiology. Recommendation. Descriptors for pure-tone audiograms. *Br J Audiol.* 1988;22(2):123.
16. Gates GA, Chakeres DW. American Academy of Otolaryngology-Head and Neck Surgery Foundation. Interpretation of diagnostic tests for acoustic neuroma. Washington, D.C.: American Academy of Otolaryngology-Head and Neck Surgery Foundation. 1988.
17. Silman S, Silverman CA. Basic audiologic testing. In: Silman S, Silverman CA. *Auditory diagnosis: principles and applications.* Singular Publishing Group. San Diego. 1997:44-52.
18. Burguetti FAR, Peloggia AG, Carvalho RMM. Limites de Audibilidade em Altas Frequências em indivíduos com queixa de zumbido. *Arq. Otorrinolaringol.* 2004;8(4):277-83.
19. Salzer TA. Neurotologic manifestations of HIV infection. *Grand Rounds Arch.* 1994;24:1-5.
20. Ceccarelli JC, Maia RA, Floriano SL, Lemos M, Bonaldi LV. Avaliação otoneurológica em pacientes HIV positivos. *Rev Bras Otorrinolaringol.* 1997;63(4):312-6.
21. Rinaldo A, Brandwein MS, Devaney KO, Ferlito A. AIDS – Related Otological Lesions. *Acta Oto-Laryngologic.* 2003;123(6):672-4.
22. Campanini A, Marani M, Mastroianni A, Cancellieri C, Vicini C. Human immunodeficiency virus infection: personal experience in changes in head and neck manifestations due to recent anti-retroviral therapies. *Acta Otorhinolaryngol Ital.* 2005;25(1):30-5.
23. Vieira ABC, Greco DB, Teófilo MMM, Gonçalves DU. Manifestações otoneurológicas associadas à terapia anti-retroviral. *Rev Soc Bras Med Trop.* 2008;41(1):65-9.
24. Vieira ABC, Mancini P, Gonçalves DU. Doenças infecciosas e perda auditiva. *Rev Med Minas Gerais.* 2010;20(1):102-6.
25. Carvalho MFP, Tidei R, Ribeiro FAQ. Surdez súbita em AIDS. *Rev Bras Otorrinolaringol.* 2001;67(2):249-51.
26. Somefun A, Nwawalo CC, Okeowo PA, Ogban LU, Akanmu AS, Okanny CC, Akinsete I. Otorhinolaryngological manifestations of HIV/AIDS in Lagos. *Niger Postgrad Med J.* 2001;8(4):170-4.
27. Domenech J, Fuste J, Traserra J. Equilibrium and auditory disorders in patients affected by HIV-1. *Rev Neurol.* 1996;24(136):1623-6.
28. Sauvaget E, Kici S, Petelle B, Kania R, Chabriat H, Tran Huy P. Vertebrobasilar Occlusive Disorders Presenting as Sudden Sensorineural Hearing Loss. *Laryngoscope.* 2004;114(2):327-32, <http://dx.doi.org/10.1097/00005537-200402000-00028>.
29. Matas CG, Marcon BA, Silva SM, Gonçalves IC. Avaliação auditiva na Síndrome da Imunodeficiência Adquirida. *Rev Soc Bras Fonoaudiol.* 2010a;15(2):174-8, <http://dx.doi.org/10.1590/S1516-80342010000200005>.
30. Roland Jr JT, Alexiades G, Jackman AH, Hillman D, Shapiro W. Cochlear Implantation in Human Immunodeficiency Virus – Infected Patients. *Otol&Neurotol.* 2003;24(6):892-5.
31. Rey D, L'Héritier A, Lang JM. Severe ototoxicity in a health care worker who received postexposure prophylaxis with stavudine, lamivudine, and nevirapine after occupational exposure to HIV. *Clin Infect Dis.* 2002;34(3):418-9, <http://dx.doi.org/10.1086/324368>.
32. Marra CM, Wechkin HA, Longstreth WT Jr, Rees TS, Syapin CL. Hearing loss and anti-retroviral therapy in patients infected with HIV-1. *Arch Neurol.* 1997;54(4):407-10, <http://dx.doi.org/10.1001/archneur.1997.00550160049015>.
33. Simdom J, Watters D, Bartlett S, Connick E. Ototoxicity associated with use of nucleoside analog reverse transcriptase inhibitors: a report of 3 possible cases and review of the literature. *Clin Infect Dis.* 2001; 34(3):2100-2.
34. Wang Y, Yang H, Dong M. The hearing manifestations of 350 patients of AIDS. *Lin Chuang Er Bi Yan Hou Ke Za Zhi.* 2006;20(22):1020-1.
35. Juan KR. Avaliação audiológica, eletroacústica e eletrofisiológica da audição em adultos com HIV/AIDS [dissertação]. 2009. São Paulo: Faculdade de Medicina, Universidade de São Paulo.
36. Matas CG, Santos Filha VAV, Juan KR, Pinto FR, Gonçalves IC. Manifestações audiológicas em crianças e adultos com AIDS. *Pró Fono Revista de Atualização Científica.* 2010b;22(3):269-74, <http://dx.doi.org/10.1590/S0104-56872010000300019>.
37. Prasad HKC, Bhojwani KM, Shenoy V, Prasad SC. HIV manifestation in otolaryngology. *Am J Otolaryngol.* 2006;27(3):179-85.
38. Williams B. Ototoxicity may be associated with protease inhibitor therapy. *Clin Infect Dis.* 2001;33(12):2100-01, <http://dx.doi.org/10.1086/324361>.
39. Kohan D, Hammerschlag PE, Holliday RA. Otologic disease in AIDS patients: CT correlation. *Laryngoscope.* 1990;100(12):1326-30.