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LARYNGEAL SYMPTOMS AND VIDEOLARYNGOSCOPY FINDINGS IN PEOPLE LIVING WITH HIV/AIDS IN THE CENTRAL AMAZON REGION: A CASE ANALYSIS

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ABSTRACT

Introduction: More than eighty percent of patients infected with the human immunodeficiency virus (HIV) will eventually develop ear nose and throat (ENT) manifestations, of which, 45% are associated with laryngeal symptoms. **Objective:** This study seeks to describe laryngeal symptoms and videolaryngoscopy findings in people living with HIV/AIDS (PLHIV) treated in a tertiary public health unit in Manaus, Amazonas, Brazil from March to May 2019. **Methodology:** A descriptive cross-sectional study that evaluated, through questionnaires and videolaryngoscopy (VDL), pharyngolaryngological complaints and laryngeal findings of PLHIV treated in the emergency care department. **Results:** A total of 34 patients reported pharyngolaryngological complaints: hawking (45%), hypopharyngeal secretion (43.3%) and globus pharyngeus (35%). Of the 60 patients, 56 were on antiretroviral therapy (93.3%), and twenty-four (40%) patients had a CD4 count of > 500 cells/mL, followed by 17 (28.3%) with a count of < 200 cells/mL. VDL was altered in 58 individuals, with the most prevalent findings being posterior edema (77%), supraglottic hyperemia (70%) and vallecula salivary stasis (37%). **Conclusion:** There was no correlation between pharyngolaryngological complaints and videolaryngoscopy findings with CD4 count or the viral load of the analyzed patients.

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INTRODUCTION

In 2017, infection by the human immunodeficiency virus (HIV), which is considered a global pandemic, affected a total of 36.9 million people.In Brazil, from 1980 to June 2018, 926,742 cases of AIDS were reported, with an annual record of approximately 40,000 new cases in the last five years. Of all the states, in 2016, the state of Amazonas presentedthe third highest rate of AIDS detection, with 30 cases/100,000 inhabitants (IACOVOU *et al.*, 2012; DAMTIE *et al.*, 2013; WHO, 2018; BRASIL, 2017; 2018a). Among the symptoms presented by patients during the natural history of this disease, 80% are of ENT manifestations, with oral manifestations being the most frequent, followed by cervical, sinonasal and, less commonly, otological involvement. The most common alteration in the oropharynx and larynx of patients living with HIV/AIDS (PLHIV) is candidiasis and, among the symptoms, the most prevalent are those associated with changes in the voice and hoarseness, which occur in 45% of cases (PRASAD *et al.,* 2006; SANJAR *et al.*, 2011; IACOVOU *et al.*, 2012; VISWANATHA, KRISHNA, 2012; JAFARI *et al.*, 2012).

As such, it is up to otorhinolaryngologists, usually the first physician to detect lesions in the pharynx and larynx, to have adequate knowledge about HIV-related alterations as well as their different forms of presentation, and provide early diagnosis and timely treatment, thus increasing the quality of life and survival of these patients (SHUSHAN *et al.,* 2009; LIFSON, LANDO, 2012; HESSOL, STRICKLER, 2017; NOUJEIM *et al.*, 2017; SIMO *et al.,* 1998). Since laryngopharyngeal reflux (LPR) is a prevalent condition in outpatients who visit the otorhinolaryngology clinic, with many controversies regarding its diagnosis and follow-up, it was necessary to use clinical instruments that can diagnose individuals and monitor the results of their treatment (SILVA *et al*., 2021).

Nevertheless, endoscopic alterations, especially laryngeal, can be found by other health professionals in several chronic diseases, such as rheumatological ones. Thus, the use of ERFS is important in the diagnosis and follow-up in all clinical phases of the diseases (SILVA, SANTOS, SEBBEN, MORAIS, 2021).

MATERIALS AND METHODS

A descriptive cross-sectional study that evaluated, through questionnaires and videolaryngoscopy, the symptoms and laryngeal alterations in people living with HIV/AIDS treated between March and May of 2019 at the emergency care departmentof the Fundação de Medicina Tropical Dr. Heitor Vieira Dourado (FMT-HVD), which is a tertiary public health unit in Manaus.Specifically, clinical, and epidemiological data (age, sex, comorbidities, medication in use) were analyzed. The laryngeal symptoms of patients were described and the findings of videolaryngoscopy were evaluated; and, later, these data were correlated with the viral load and CD4 count of these patients.For the identification of laryngeal symptoms, the reflux symptom index (RSI) was used and for the evaluation of videolaryngoscopy findings, the endolaryngeal reflux findings scale (ERFS). These are easily understood by patients and easily applied by otolaryngologists, respectively. The sample included 99 patients and was calculated using the equation of Box and Hunter (1978) considering the number of patients living with HIV/AIDS treated in the same period of the previous year (March to May 2018) (N: 5,206, p: 7%, q: 93%, d: 5%; z: 1,96). The PLHIV attended with or without pharyngolaryngological complaints and who fitted the inclusion criteria of this study, were invited to participate in the research and asked to complete the questionnaire and perform the tests. Of the patients referred, only 60 patients agreed to participate in the research. Patients, older than 18 years of age, diagnosed with HIV infection through diagnostic tests, using or not antiretroviral therapy (ART). Pregnant women, indigenous people, smokers, narcoticsusers, and patients with chronic upper or lower airway diseases and those unable to perform videolaryngoscopy were excluded from the present study.

RESULTS

A total of 60 patients agreed to participate in this study, with a male (56.7%; N=34) and female (43.3%; N=26) ratio of 1.3:1. There was a variation in age from 21 to 73 years, with an average of 40.9 years (± 12.7 years), with the most prevalent age group being 41 to 50 years of age (30%; N=18). Thirty-four (57%) of the sixty patients presented pharyngolaryngological complaints, with the most frequent symptoms being hawking (45%; N=27), hypopharyngeal secretion (43.3%; N=26) and globus pharyngeus(35%; N=21), followed by hoarseness (31.7%; N=19) and cough with secretion (28.3%; N=17) (Figure I).

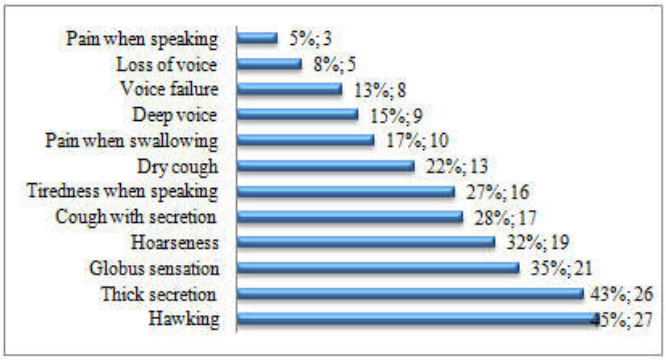

Figure 1. Symptoms presented by patients living with HIV/AIDS tested at a tertiary health unit in Manaus, AM

Regarding the length of time since diagnosis of HIV infection, 38.3% (N=23) of the patients reported less than 5 years, while 35.5% (N=21) had received their diagnostic confirmation between 5 and 10 years ago. The mean length of time since HIV diagnosis was 7.7 years.A total of 93.3% (N=56) of the individuals analyzed reported the use of antiretroviral therapy. Of the 60 patients, 4 did not use antiretroviral therapy. According to the number of CD4/mm^3 cells, there was a variation of 11 to 1,727 cells/mm^3 in the studied population, with an average of 495.4 cells/mm^3 (standard deviation 405.3).

Almost half of the patients (40%; N=24) had a CD4 count greater than 500 cells/mm^3, followed by the group of patients with a count of less than 200 cells/mm^3 (28.3%; N=17). Half (50%; N=14) of the patients with an undetectable viral load (<20 copies/mL) had pharyngolaryngological complaints. Of the 4 individuals with a viral load greater than 1 million copies/mL, 3 (75%) reported complaints in the pharynx and/or larynx. However, our study found no evidence of correlation between viral load and pharyngolaryngological complaints of patients at a 5% confidence level. Pharyngeal and/or laryngeal symptoms were observed in 10 (59%) patients with CD4 < 200 cells/mm^3, in 3 (33%) patients with CD4 > 200 ~350 cells/mm^3, in 8 (80%) of those with a count between > 350 ~500 cells/mm^3 and in 13 (54%) of those with CD4 > 500 cells/mm^3. However, there was no evidence of correlation between CD4 and the patients' pharyngolaryngological complaints at a 5% confidence level.

The most frequent symptoms per CD4 range are described in Table I. Hawking, thick secretion and globus were the main symptoms reported, regardless of the CD4 count in these patients. Only 3% (N=2) of the patients had a VDL exam without alterations. The remaining 97% showed alterations in the pharynx and/or larynx region. In the oropharynx, the most frequent findings were hypertrophy of the lymphoid follicles (12%; N=7), pseudomembranous candidiasis (3%; N=2) and hypertrophy of the palatine tonsil (3%; N=2) (Table II). Posterior edema, supraglottic hyperemia and vallecula salivary stasis were the most frequent findings in the hypopharynx, which were found in 77% (N=46), 70% (N=42) and 37% (N=22) of patients, respectively; followed by pseudomembranous candidiasis, ventricular band hyperconstriction, parallel cleft, fusiform cleft, vocal fold hyperemia and vasculodysgenesis, with 3% (N=2) each (Table II). VDL was altered in 33 (97%) of the 34 patients with oropharyngolaryngological complaints. In 25 (96%) of the 26 patients without complaints, no changes were observed in the endoscopic examination (VDL). The examination was normal in 1 (3%) patient of the complaining group and in 1 (4%) patient of the group without complaints.Both patients with normal VDL had CD4 counts greater than 500/cells/mm^3. Regarding the viral load of these two individuals, one had a total HIV RNA of between 20 and 40 copies/mL and the other recorded less than 20 copies per milliliter of blood. There was no agreement between the finding of alteration in the videolaryngoscopy exam and viral load levels or between these findings and the CD4 count of the 60 patients.

DISCUSSION

The most prevalent age groups in our study, 41-50 years (30%, N=18) and 31-40 years (28.3%, N=17) differ from that found in the findings of the Brazilian Ministry of Health (2018a), which showed greater involvement of a younger audience (between 20 and 34 years); however, our data corroborated the findings of Prasad *et al*. (2006), in which most patients were between 31 and 40 years of age. Studies have shown that 80% of HIV-infected individuals presented ENT symptoms during infection, which is associated with disease progression and failure in HIV treatment (JAFARI *et al*., 2012). Jafari *et al*. (2012) described the presence of laryngeal symptoms in 45.9% of the 98 patients analyzed, the most common being vocal alterations (23.5%) and hoarseness (17.3%). Prasad *et al*. (2006) reported cough with sputum as the most common symptom in his study, occurring in 64% of patients.In our participants, 57% reported some type of laryngopharyngological complaint, a slightly higher number than the study mentioned above. Among the symptoms, hawking was in first place, with a prevalence of 45%, followed by secretion in the hypopharynx (43.3%) and globus pharyngeus(35%). A significant number of patients in our study (93.3%; N=56) were using ART, a prevalence higher than that presented at the national level in 2018, which was 75%, according to a report by the Ministry of Health (MS). The use of ART can cause a considerable decline in the rates of otorhinolaryngological manifestations due to a high CD4 count (BRASIL, 2018; JAFARI *et al*., 2012).

Table 1. Distribution of laryngopharyngological symptoms as a function of CD4 cell count in patients living with HIV/AIDS tested at a tertiary health unit in Manaus, AM (in cells/mL)

Symptoms	CD4									
	≤ 200		> 200 ≤ 350		> 350 ≤ 500		> 500		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Hawking	6	22.2%	3	11.1%	6	22.2%	12	44.4%	27	45.0%
Thick secretion	6	23.1%	2	7.7%	4	15.4%	14	53.8%	26	43.3%
Globus sensation	6	28.6%	2	9.5%	5	23.8%	8	38.1%	21	35.0%
Hoarseness	5	26.3%	1	5.3%	5	26.3%	8	42.1%	19	31.7%
Cough with secretion	5	29.4%	3	17.6%	4	23.5%	5	29.4%	17	28.3%
Tiredness	6	37.5%	2	12.5%	5	31.3%	3	18.8%	16	26.7%
Deep voice	2	15.4%	3	23.1%	3	23.1%	5	38.5%	13	21.7%
Pain when swallowing	3	30.0%	1	10.0%	4	40.0%	2	20.0%	10	16.7%
Deep voice	3	33.3%		0.0%	3	33.3%	3	33.3%	9	15.0%
Voice failure	3	37.5%		0.0%	1	12.5%	4	50.0%	8	13.3%
Loss of voice	2	40.0%		0.0%	1	20.0%	2	40.0%	5	8.3%
Pain when speaking	2	66.7%		0.0%	1	33.3%		0.0%	3	5.0%

Table 2. Findings of the videolaryngoscopy exam in the oropharynx and hypopharynx region in patients living with HIV/AIDS tested at a tertiary health unit in Manaus, AM

Finding	No. of Patients	%
Oropharynx		
Lymphoid follicles	7	12%
Hypertrophy of the amygdala	2	3%
Candidiasis	2	3%
Hypertrophy of lingual tonsils	1	2%
Hyperemia ofthe pharynx	1	2%
Epiglottitis	1	2%
Hypopharynx		
Posterior edema	46	77%
Supraglottic hyperemia	42	70%
Salivary stasis in vallecula	22	37%
Candidiasis	2	3%
Ventricular band hyperconstriction	2	3%
Parallel cleft	2	3%
Fusiform cleft	2	3%
Hyperemia of vocal folds	2	3%
Vasculodysgenesis	2	3%
Hyperemia in hypopharynx	1	2%
Salivary stasis in hypopharynx	1	2%
Bulging in ventricular band	1	2%
Triangular cleft	1	2%
Vocal nodules	1	2%
Vocal polyp	1	2%
Laryngeal papillomatosis	1	2%
Pachydermy	1	2%

In the study of Venkat *et al*. (2008), which analyzed the profile of 356 PLHIV treated in a federal referral clinic for HIV in 2006, 13.8% patients had a CD4 count of between 0-200 cells/mm^3, 17.4% between 201-350 cells/mm^3 and 54.5% had more than 350 cells/mm^3. 14.3% of the patients did not have this data. Our findings differ from the above study only in the CD4 range between 0-200 cells/mm^3, for which we obtained more than twice as many patients (28.3%) with this CD4 count. Higher viral loads are associated with greater transmissibility, potential for faster disease progression and more advanced disease. When levels are above 100,000, this is considered a strong justification for initiating antiretroviral therapies (RIO DE JANEIRO, 2015). In this study, 9 of the 60 patients (15.0%) had a viral load greater than 100,000 copies/mL and, in 4 cases, it was greater than 1,000,000 copies/mL. Venkat *et al*. (2008) recorded a total of 9.3% of the 356 patients studied with an average viral load above 100,000 copies/mL. In their studies, Tappuni and Fleming (2001) and Iacovou*et al*. (2012) reported that the prevalence of otorhinolaryngological manifestations was significantly related to CD4 count and viral load greater than 3,000 copies/mL, both in patients on antiretroviral therapy and in those without it. Our results, however, showed no statistical correlation between the presence of symptomatology and the level of viral load of patients. Of a group of 98 patients with ENT complaints, Jafari *et al*. (2012) reported that 42.9% of them had CD4 counts less than 200 cells/mL. Our research, unlike the above study, included only pharyngolaryngological complaints and presented a uniform distribution of patients with symptomatology among the different CD4 ranges. Patients with complaints in the pharynx and/or larynx had a greater number than those without complaints, at all CD4 levels except in the group between 200 and 350 cells/mL of blood, in which individuals without symptoms predominated. These findings, however, were not statistically significant (p = 0.23026). However, it is emphasized that the dosage of CD4 and the viral load accepted for the present study included tests performed in the period of up to 6 months prior to videolaryngoscopy exams, which may not represent the immunological status and quantification of the HIV RNA of these patients at the time of the interview and the examination. More than 80% of patients with HIV infection will eventually develop ENT manifestations, although their incidence has been reduced with the advent of highly active antiretroviral therapy (HAART). Through this study, it is emphasized that, unlike the symptoms and oral findings with extensive reports in the national and international literature, laryngeal involvement has been reported to considerably less extent (IACOVOU *et al*., 2012; TINELLI *et al.,* 1995; TAMI *et al.*, 1999). Maurya *et al*. (2013) described oropharyngeal candidiasis as the most common opportunistic infection in HIV-infected patients, and it is estimated that more than 90% of HIV-positive patients will develop this infection at some point during the progression of the disease. In the work of Prasad *et al*. (2006), it was the most common oropharyngeal finding, affecting 39% of individuals.

Tshifularo *et al*. (2013) reported that 12.34% (N=19) of his patients had oral candidiasis, with pseudomembranous candidiasis as the most common subtype (83%). Our results, however, reveal candidiasis in the oropharynx and larynx of only 3% of those evaluated. Of the 24 laryngeal alterations found by Arriola *et al*. (2015) among the 301 PLHIV analyzed by them, laryngopharyngeal reflux (LPR) (N=11) and acute laryngitis (N=5) stand out. In agreement with these results, our research pointed to posterior laryngeal edema (77%) and supraglottic hyperemia (70%), signs of LPR according to Vaezi *et al*. (2003), as the most prevalent findings for LDV. In the heterogeneous group of rheumatological diseases, the laryngeal findings are consistent with the alterations exposed in our study. Posterior edema occupies first place with 70%, and supraglottic hyperemia and arytenoid mucosal edema have a frequency of 65% and 60%, respectively (SILVA, SANTOS, SEBBEN, and MORAIS, 2021). The laryngeal hyperemia present in videolaryngoscopy exams of 35 subjects with objective diagnosis of LPR was the only item that showed improvement (43.5%) after treatment with 90 days of proton pump inhibitor, while the other findings (subglottic edema, ventricular obliteration, vocal fold edema, hypertrophy of the interarithenoid region, granuloma and mucus) remained unaltered (SILVA *et al*., 2021).

To date, no study in the national or international literature has analyzed the correlation between the pharyngolaryngological symptoms reported by patients and laryngoscopy findings viaVDL in PLHIV. In our study, almost all patients with complaints (33/34) and those without pharyngeal and/or laryngeal symptomatology (25/26) presented alterations on examination by videolaryngoscopy.Plasma HIV-RNA levels greater than 3,000 copies/mL are one of the predictors of ENT manifestations in HIV-positive patients (IACOVOU *et al*., 2012). The only two patients, in the present study, without changes to VDL had viral loads of less than 40 copies/mL. Damtie *et al*. (2013) stated that the prevalence of opportunistic infections is higher among HIV-infected patients with CD4 levels below 200/mm^3, followed by those with a count between 200-350/mm^3. Data confirmed by a study conducted by Arriola *et al*. (2015), in which ENT manifestations were observed in 16 patients with CD4≥ 500 cells/mm^3, in 26 with CD4 of 350-499 cells/mm^3, in 39 with CD4 of 200-349 cells/mm^{3}and in 115 with CD4 < 200 cells/mm^3.In our results, there was no reduction in patients with altered tests as their CD4 count increased; however, as reported above, the lowest number of patients with VDL alterations belonged to the group with more than 500 CD4 cells per milliliter of blood.

CONCLUSION

The most prevalent pharyngolaryngological complaints in patients living with HIV/AIDS were hawking, thick secretion and globus pharyngeus and, among the videolaryngoscopy findings, almost all patients presented supraglottic hyperemia and posterior laryngeal edema. These results raise the importance of otorhinolaryngological follow-up in this population.In our study, there was no correlation between pharyngolaryngological complaints and videolaryngoscopy findings with CD4 count or the viral load of the analyzed patients. Divergent results may be found in a study involving a greater number of patients, for a longer period and including outpatient and inpatient patients, and the causality between HIV infection and pharyngolaryngological alterations could be evaluated through a longitudinal study.

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