

Original Research Article

A study on otorhinolaryngologic manifestations in human immunodeficiency virus infected patients

Shanmuga Ashok S.¹, Rajendran S.^{2*}

¹Department of Otorhinolaryngology, Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India

²Department of Otorhinolaryngology, Chengalpattu Government Medical College, Chengalpet, Tamil Nadu, India

Received: 17 January 2020

Revised: 01 February 2020

Accepted: 03 February 2020

***Correspondence:**

Dr. Rajendran S.,

E-mail: rajendran24253@gmail.com

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ABSTRACT

Background: The main aim of this study was to find out the ear, nose, and throat (ENT) manifestations in a selected regional population of 100 HIV infected patients, to identify the commoner ENT manifestations among them and to make these manifestations, a guide for regional ENT surgeons, to diagnose HIV/AIDS patients early and to treat them accordingly.

Methods: The study was a prospective study which was conducted for a period of five years which included 100 HIV seropositive patients, among the patients attending the Outpatient Department of the Otorhinolaryngology and anti-retroviral therapy centre across Government Hospitals in Tamil Nadu according to our inclusion or exclusion criteria. Detailed ENT clinical examination as well as laboratory investigations were carried out to evaluate the nature of ENT presentations of HIV infection.

Results: Out of the 100 HIV positive patients, who had some form of ENT symptoms, the most common ENT manifestation in HIV/AIDS was oral candidiasis (40%) followed by cervical lymphadenopathy (30%). Other common manifestations are oral herpes simplex and sensorineural hearing loss. Less common manifestations are chronic sinusitis, tuberculous laryngitis, chronic otitis media, oral hairy leukoplakia, nasal polyps and Kaposi's sarcoma. Oral candidiasis, chronic/recurrent mucocutaneous herpes simplex, oral hairy leukoplakia and Kaposi's sarcoma are the AIDS defining illnesses. Oral hairy leukoplakia, is pathognomonic of HIV infection.

Conclusions: These manifestations help ENT surgeons, to recognize HIV/AIDS patients from the specific ENT lesions occurring in them, for early diagnosis and subsequent treatment.

Keywords: HIV, AIDS, Oral hairy leukoplakia, Kaposi sarcoma, Oral candidiasis, Tubercular laryngitis

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS), caused by the human immunodeficiency virus (HIV) is a major public health problem and is a major killer throughout the world. It is the biggest challenge for the medical community to treat and effectively cure the disease. The ear, nose, and throat (ENT) and head and neck surgeons have the main responsibility in the earlier recognition of head and neck manifestations of HIV infection and to

treat accordingly so that these patients are diagnosed early and receive appropriate care. It was reported initially that 41 percent of patients with AIDS had head and neck manifestations.¹ As awareness has increased, however, recognition of these lesions has also increased, until now it seems that nearly all patients with AIDS have head and neck manifestations.

Some AIDS defining ENT manifestations are chronic or recurrent oropharyngeal candidiasis, chronic recurrent

mucocutaneous herpes simplex, oral hairy leukoplakia and oral or aural Kaposi's sarcoma.²⁻⁴ Of these, oral hairy leukoplakia is virtually pathognomonic of HIV disease.⁵ Though kaposi's sarcoma is rare in our country, it is an AIDS defining illness and we should suspect HIV infection in those individuals with Kaposi's sarcoma. It is very common in African homosexual men. It has to be noted that the studies regarding the prevalence of these AIDS defining ENT manifestations among Indian population has been very meagre. With these in mind our main aim of this study was to find out the ENT manifestations in a selected regional population of 100 HIV infected patients, to identify the commoner ENT manifestations among them and to make these manifestations, a guide for regional ENT surgeons, to diagnose HIV/AIDS patients early and to treat them accordingly.

METHODS

The study was an observational study which was conducted for a period of five years from January 2015 to January 2019 after approval from institutional Ethical committee. The study included 100 HIV seropositive patients, among the patients attending the Outpatient Department of the Otorhinolaryngology and anti-retroviral therapy (ART) centre across five Government Hospitals in South India, details of each institution with duration of study carried out in that institution has been shared in Table 1. Detailed ENT clinical examination as well as laboratory investigations were carried out to evaluate the nature of ENT presentations of HIV infection. Patients included in our study were previously proved seropositive HIV infected patients of age group

20 to 50 years of both sexes with some form of ENT symptoms like oral white patches, painful oral ulcers, neck swelling, headache, nasal obstruction, nasal discharge, ear pain/ discharge, dysphonia, throat pain, swelling in mouth or difficulty in swallowing. HIV infected patients with no obvious ENT symptoms, HIV infected patients with coexisting diabetes mellitus, HIV infected patients received or receiving steroids or any other immunosuppressive therapy and HIV infected patients with past history of hard of hearing and those patients who were previously diagnosed to have chronic suppurative otitis media and chronic sinusitis were excluded from our study. Detailed history was taken and physical examination was done for each patient as shown in proforma. All patients underwent the following investigations i.e. blood total count, differential count, erythrocyte sedimentation rate, haemoglobin, chest X ray PA view, ELISA for HIV and CD4+ T cell count. Selected patients underwent following investigations like gram stain for oral candidiasis, biopsy for histopathological examination for oral hairy leukoplakia, Tzanck smear for oral herpes simplex infection, fine needle aspiration cytology for neck nodes, biopsy for histopathological examination for swelling in oral cavity and for suspected tuberculous laryngitis, pure tone audiogram for patients with hard of hearing, pus for culture and sensitivity (C/S) from pus in ear or middle meatus or nasal cavity through DNE and sputum AFB for suspected tuberculous laryngitis. Diagnostic nasal endoscopic examination and videolaryngoscopic examination too were carried out for all selected patients. Universal barrier precautions were followed by all health care workers and all equipments involved in our study to prevent them from getting exposed to infection.

Table 1: Distribution of cases across institutions.

Name of institutions	Number of HIV patients selected (n=100)	Percentage (%)	Duration
Government Thiruvapur Medical College, Thiruvapur	19	19	January 2017-January 2018 (2 years)
UIORL, Madras Medical College, Chennai	24	24	January 2015-January 2017 (3 years)
Stanley Medical College, Chennai	17	17	January 2018-January 2019 (2 years)
Government Medical College, Omandurar Govt Estate, Chennai	18	18	January 2018-January 2019 (2 years)
Government Chengalpet Medical College, Chengalpet	22	22	January 2018-January 2019 (2 years)

Statistical analysis

Data was compiled and analysed Microsoft excel for windows. The results were presented as percentages out of total HIV patients included.

RESULTS

Out of the 100 patients studied 66 patients were males and 34 were females (Table 2). According to Table 3, out

of 100 HIV positive patients, 66% (n=66) were between the age group of 30 to 39 years. 26% (n=26) were between the age group of 40 to 50 years, while only 8% (n=8) were between 20 to 29 years. The analysis of socio-economic status of the patients is given in Table 4. 60 of them (60%) belong to low socioeconomic group. 30 of them (30%) were of middle socioeconomic group. Only 10 (10%) of them belong to high socioeconomic group. According to Table 5, Ear manifestations were of 24%, nose, 14%, throat, 74% and neck 30%. The frequencies

of various ENT manifestations are shown in Table 6. Here 40 patients had oral candidiasis i.e. 40%, 30 (30%) of them had cervical lymphadenopathy, 20 (20%) of them had herpes simplex and another 20 (20%) had sensorineural hearing loss. 8 (8%) patients had tuberculous laryngitis. 10 (10%) patients had chronic sinusitis. 4 (4%) patients had nasal polyps, 4 (4%) had oral hairy leukoplakia and 4 (4%) others had chronic otitis media. Only 2 patients had Kaposi's sarcoma. 40 (40%) out of 100 patients had more than one ENT manifestation which are summarized in Table 7.

Table 2: Sex distribution of the selected patients.

Gender	No. of patients (n=100)	Percentage (%)
Males	66	66
Females	34	34

Table 3: Age distribution of the patients selected.

Age group (in years)	No. of patients (n=100)	Percentage (%)
20-29	8	8
30-39	66	66
40-50	26	26

Table 4: Distribution of patients according to socio-economic status.

Socio-economic status	No. of patients (n=100)	Percentage (%)
Low	60	60
Middle	30	30
High	10	10

Table 5: Frequency of ear, nose, throat and neck manifestations in HIV infection.

	Percentage (%)
Ear	24
Nose	14
Throat	74
Neck	30

Table 6: Frequency of ENT manifestations among HIV infected.

ENT manifestations	No. of patients	%
Oral candidiasis	40	40
Tuberculous laryngitis	8	8
Cervical lymphadenopathy	30	30
Chronic sinusitis	10	10
Nasal polyp	4	4
Herpes simplex	20	20
Oral hairy leukoplakia	4	4
Sensorineural hearing loss	20	20
Kaposi's sarcoma	2	2
Chronic otitis media	4	4

Table 7: Frequency of patients presented with more than one ENT manifestations.

ENT manifestations	No. of patients (n=40)
	N (%)
Oral candidiasis and sensorineural hearing loss	10 (10)
Cervical lymphadenopathy and nasal polyps	2 (2)
Cervical lymphadenopathy and sensorineural hearing loss	10 (10)
Oral candidiasis and chronic otitis media	2 (2)
Oral candidiasis and nasal polyps	2 (2)
Oral herpes simplex and chronic sinusitis	4 (4)
Cervical lymphadenopathy and oral hairy leukoplakia	2 (2)
Cervical lymphadenopathy and chronic otitis media	2 (2)
Oral candidiasis and sinusitis	4 (4)
Cervical lymphadenopathy and oral candidiasis	2 (2)

DISCUSSION

This study evaluated ENT manifestations in 100 HIV infected patients and the frequency of ENT manifestations is discussed as below. Here, as per Table 1, 66 patients were males and 34 were females. As per Table 2, 66% of patients were of the age group 30 to 39 years, 26% of patients were of the age group 40 to 50 and 8% of patients were of the age group 20 to 29 years. Hence the commonest age group, affected in this study was 30 to 39 years. This is the age group that is most economically productive in the society. They have more exposure. Also, even if they were exposed in younger age the manifestations become apparent after some years only. This could possibly be the reason why this age group is the most common affected group.

As per Table 4 the people in low socioeconomic status group were the most commonly affected. 60% of the patients belong to low socioeconomic group. 30% were of middle socioeconomic status and only 10% belong to high socioeconomic status. This is so because only low socioeconomic status people are more ignorant, illiterate and do not know or follow safe sexual practices. Also, sexually transmitted diseases (STDs) are more common in low socioeconomic group due to poor hygiene, crowding and ignorance regarding early consultation and also several myths are commoner in low socioeconomic group. Also, native and traditional treatments are followed among low socioeconomic group people commonly. STDs naturally increase the risk of transmission of HIV.

According to Table 5, throat manifestations, which comprise of oral candidiasis, oral herpes simplex, tuberculous laryngitis, Kaposi's sarcoma and oral hairy leukoplakia were the commonest (74%). Nose manifestations which comprise of chronic sinusitis and nasal polyps were of 14%. Ear manifestations which comprise of chronic otitis media and sensorineural hearing loss were of 24%. Neck manifestation which comprises of only cervical lymphadenopathy was of 30%.



Figure 1: Oral candidiasis.

According to Table 6, the most common ENT manifestation among 100 HIV infected patients happened to be oral candidiasis which occurred in 40 (40%) patients. Candidiasis (Figure 1) is the most common fungal infection in patients with AIDS. Out of the 100 patients studied 40% had oral candidiasis. We have got 3 types of oral candidiasis occurring in HIV infected patients - pseudomembranous candidiasis, erythematous candidiasis and hypertrophic candidiasis. Here the most common type observed was pseudomembranous candidiasis which occurred in 80% (n=32), erythematous candidiasis occurred in 15% (n=6) and only 5% (n=2) had hypertrophic candidiasis. According to Singh et al oral candidiasis occurred in 22.5% of HIV infected patients they studied.⁶ As per Hadjivassilou et al oral candidiasis occurred in 61% of HIV infected patients they studied.⁷ 60% of the HIV infected patients had oral candidiasis in a study by Forsters et al.⁸ According to Ibara et al 14.6% of HIV infected patients had oral candidiasis.⁹ Oral candidiasis is one of the earliest and most frequent of the opportunistic infections in patients with HIV/AIDS.

One of the earliest signs of HIV infection is persistent generalized lymphadenopathy, also known as HIV lymphadenopathy. This entity is defined as unexplained generalized lymphadenopathy, involving two or more extra inguinal sites and lasting more than three months. In our study, 30% of the patients had cervical lymphadenopathy out of which 4% had tuberculous lymphadenitis. Most of the patients had non-specific chronic inflammatory reaction and some had reactive hyperplasia of lymph nodes. According to Hadjivassilou et al, 49% of HIV infected patients had cervical lymphadenopathy.⁷ As per Forsters et al, 27% of HIV patients had cervical lymphadenopathy.⁸

Herpes simplex infections occur at a higher frequency in the HIV-positive population than in the general population. Of the two subtypes, HSV-1 and HSV-2, the former is far more commonly the causative agent of lesions in the oral cavity. Herpes labialis is the most common presentation of this infection. In HIV-infected patients, however, these lesions are larger and more numerous, recur more frequently and last longer than such lesions in HIV-negative patients. The lesions appear as ulcerations with raised borders and are painful and tender to touch. In our study 20% of the patients had oral herpes simplex lesions. According to Reiderer et al, 10% of HIV positive patients had oral herpes simplex.¹⁴ They occur on heavily keratinized mucosal surfaces. Tests of the borders of the ulcer using Tzanck preparation, or viral cultures, help in confirming the diagnosis.

Sensorineural hearing loss had occurred in 20% of the HIV positive patients studied. All of them had mild to moderate type of sensorineural hearing loss. It could be argued that in general, otologic manifestations are less common than other head and neck manifestations. Some of the more common complications include otitis externa, serous otitis media, Kaposi's sarcoma, eustachian tube obstruction secondary to nasopharyngeal mass, acoustic brainstem response abnormalities and sensorineural hearing loss secondary to central nervous system complications. Since HIV is a known neurotropic virus, sensorineural hearing loss may be explained by direct involvement of the eighth cranial nerve, although no pathologically documented case has been reported. On the other hand, central nervous system complications of AIDS, such as cryptococcal meningitis or neurosyphilis, can also cause sensorineural hearing loss. Sensorineural hearing loss is among the numerous neurologic manifestations of AIDS. The hearing loss may be a result of an infectious complication of AIDS, particularly cryptococcal meningitis or syphilis, or as a primary neurologic manifestation of the disease. HIV should be a consideration in patients with otherwise unexplained sensorineural hearing loss when risk factors are present. In this study only pure tone audiogram was done to assess the degree and type of hearing loss.

A total of 8% of the patients had chronic sinusitis which was diagnosed with the help of diagnostic nasal

endoscopy and computed tomography (CT) of paranasal sinuses. According to Singh et al, 27.5% of HIV positive patients had chronic sinusitis.⁶ According to Ibara et al, 14.2% of HIV positive patients had chronic sinusitis.⁹ The prevalence of rhinosinusitis ranges from 20 to 70 percent in patients with AIDS. Sinusitis is a spectrum of inflammatory diseases involving the nose and paranasal sinuses. This spectrum includes acute and chronic sinusitis, with or without mucopurulent postnasal drainage. The organisms that cause acute sinusitis in both immunocompromised and immunocompetent populations include *Streptococcus pneumoniae* and *Haemophilus influenzae*. *Staphylococcus aureus* and *Pseudomonas aeruginosa* are more commonly associated with chronic sinusitis. Just as in hosts without HIV infection, HIV-positive patients with sinusitis have signs and symptoms of fever, general and localized headaches, and mucopurulent drainage from sinus ostia. Computed tomographic (CT) scan of the sinuses determines the extent of disease. Patients with AIDS appear to have an increased incidence of sinusitis, although most reports are anecdotal. In addition to the usual organisms of sinusitis.

AIDS patients have an increased likelihood of culturing *Pseudomonas* and unusual organisms such as *Legionella pneumophila* and *Pneumocystis carinii*. Cases of invasive fungal sinusitis in patients with AIDS are not unusual, but the overall incidence of fungal sinusitis is unknown. AIDS patients with low CD4 counts may show evidence of hyper-IgE conditions, including allergic rhinitis with severe congestion and thick nasal secretions. In this study, pus from middle meatus and nasal cavity was taken and a study of culture made. The organisms found out were *S. pneumoniae*, *H. influenzae* and *Proteus*.

A total of 4% of patients had tuberculous laryngitis which was diagnosed based on clinical features, history and histopathological examination of suspected lesions of larynx. According to Lee et al, 12% of HIV positive patients had tuberculous laryngitis.¹⁰ As per Cantwell et al, 30% of HIV patients had pulmonary tuberculosis and only 6% had tuberculous laryngitis.¹¹ It is estimated that tuberculosis is 100 to 500 times more common in HIV-positive patients. This is not surprising because the main defense against mycobacteria is cell mediated immunity. The most common symptoms were hoarseness, odynophagia and shortness of breath. The majority of the patients had white exophytic lesions which may involve any area of the larynx and looked like carcinoma or chronic laryngitis. Systemic symptoms such as fever, night sweats, and weight loss are very common in AIDS patients and coupled with other illnesses masked the possibility of laryngeal disease. This may delay the diagnosis of laryngeal tuberculosis. The diagnosis is made by tissue examination and culture. Polymerase chain reaction identifying tuberculous DNA shows potential in making this diagnosis more rapidly. Cultures should be obtained to determine drug susceptibility because of the high incidence of multi-drug resistant tuberculosis. 90% of cases of laryngeal tuberculosis are

associated with active pulmonary tuberculosis making this a contagious illness. Therefore, patient isolation is needed as long as the patient has potentially infectious sputum. Adequate room ventilation/filtration and masks for all health care providers are necessary. The individual must have a chest X-ray and a PPD test (although many AIDS patients are allergic) to check for active tuberculosis. The most common presenting symptom of laryngeal tuberculosis is hoarseness, with a high percentage of patients also reporting dysphagia, odynophagia, cough, and weight loss. 20 to 40% of patients show no evidence of pulmonary involvement, but purified protein derivative is usually positive. Almost any area of the larynx can be involved as well as supraglottic structures such as the aryepiglottic folds and epiglottis. Lesions range from areas of nonspecific inflammation to a nodular, exophytic lesion or mucosal ulcerations. Histopathological examination of biopsied tissue revealed tubercles consisting of a homologous caseous centre (staining red with eosin), a periphery of pale epithelial cells containing one or more giant cells, and an outer zone of lymphocytes.

Around 4% of 100 HIV patients had chronic otitis media which was diagnosed based on history, clinical examination. Pus was taken and culture of the pus done. According to Shapiro et al, 15% of HIV patients had chronic otitis media.¹² According to Rarey et al, 2% of HIV patients had chronic otitis media.¹³ Serous otitis media, (i.e., middle ear effusion without inflammation) is more prevalent in the adult AIDS population than in the general population. It can result from a malfunctioning eustachian tube secondary to recurrent viral infections, adenoidal hypertrophy, nasopharyngeal tumors or allergies. Unilateral or recurrent serous otitis media warrants evaluation of the nasopharynx to rule out large benign or malignant nasopharyngeal tumors. These lesions present as nasal obstruction, hearing loss, otitis media and recurrent serous otitis media. The presence of large lymphoid proliferation of the adenoids in a patient should prompt the physician to obtain a good history of risk factors and to perform serologic testing for HIV. Acute otitis media is common in patients with AIDS. Symptoms, causative agents and treatment of acute otitis media are similar in patients with AIDS and in the general population. The predominant agents are *S. pneumoniae*, *H. influenzae* and *Moraxella catarrhalis*. Otitis media and mastoiditis caused by *Pneumocystis carinii* are uncommon opportunistic otologic infections unique to patients with AIDS. An aural polyp is frequently found in the external auditory canal or middle ear that, on biopsy, reveals a typical *P. carinii* cyst if stained with Grocott-Gomori methenamine silver nitrate. *P. carinii* gains access to the middle ear in three ways: (1) it can extend retrogradely through the eustachian tube from a colonized nasopharynx, (2) it can spread medially from the external auditory canal or (3) it can seed the temporal bone hematogenously.

In this study 4% of the patients had nasal polyps which turned out to be fungal sinusitis on doing fungal staining. According to Lee et al, 8% of HIV patients had fungal sinusitis with nasal polyps. According to Shapiro et al, 5% of HIV patients had nasal polyps.¹² Causative organisms include atypical opportunistic organisms as well as agents responsible for sinusitis in hosts without AIDS. Opportunistic fungal sinusitis is caused by organisms such as *Alternaria alternata*, *Aspergillus*, *Pseudallescheria boydii*, *Cryptococcus* and *Candida albicans*.



Figure 2: Oral hairy leukoplakia.

4% of the patients had oral hairy leukoplakia (Figure 2) which was diagnosed based on history, characteristic clinical feature and histopathological examination. According to Hadjivassilou et al 24% of HIV positive patients had oral hairy leukoplakia.⁷ According to Riederer et al, 5% of HIV patients had oral hairy leukoplakia.¹⁴ Hairy leukoplakia is a newly recognized, coarsely textured lesion of the oral cavity, unique to HIV-positive persons. It is a white lesion that forms most often on the lateral borders of the tongue. The lesion is raised, cannot be scraped off and has a hairy appearance. It resembles the hyperplastic form of candidiasis that is refractory to antifungal therapy. The lesion often indicates progression to full-spectrum AIDS. *Epstein-Barr* virus has been suggested as the causative agent.

In this study, about 2% of patients had kaposi's sarcoma diagnosed by history, typical clinical appearance, site and histopathological examination. This patient had smooth, pink, fleshy irregular mass over the left side of the hard palate which has been shown in the photograph attached. On taking biopsy from the lesion, the histopathological feature confirmed Kaposi's sarcoma. The patient is a known case of AIDS, under ART. His CD4+ T cell count was 50 cells/cu.mm. According to Hadjivassilou et al, 12% of HIV patients had kaposi's sarcoma.⁷ According to Herdman, et al, 26% of HIV patients had Kaposi's sarcoma which is by far the most common oral neoplasm in AIDS patients.⁸ It is more common among homosexual

and bisexual males with AIDS than in persons who contracted the HIV virus from any other source. Kaposi's sarcoma in patients under 60 years of age almost always indicates AIDS and fulfills the centers for disease control and prevention's requirement for the definition of AIDS. The palate serves as the site for 95 percent of these oral lesions, while any other mucosal surface of the mouth can also be a site. In the early stages, the lesions are macular, dark or erythematous, maturing into more raised and lobulated mucosa. The lesions can ulcerate but rarely bleed or become tender. Kaposi's sarcoma is usually slow to develop but, in some reported cases, the lesions rapidly disseminate to involve the thoracic and abdominal viscera. Symptoms include increasing pain, odynophagia, dysphagia and difficulty in mastication. The epidemic form of Kaposi's sarcoma is associated with AIDS. It presents with skin lesions anywhere and disseminate to mucous membranes, GI tract, lymph nodes and viscera. In the early stages, irregular dilated epidermal vascular spaces, extravasated red cells and hemosiderin are characteristic in histological examination. This histologic appearance is very similar to that of granulation tissue or stasis dermatitis. Later in the disease process, more characteristic lesions show spindle cells around slit spaces with extravasation of erythrocytes. In contrast, irregular vascular spaces lined by nests of uniform cells describes the histologic appearance of glomus tumor, while multiple dilated endothelial lined vessels that lack red blood cells.

CONCLUSION

To conclude, our study findings have showed that the most common ENT manifestation in Tamil Nadu patients having HIV/AIDS were oral candidiasis followed by cervical lymphadenopathy, oral herpes simplex and sensorineural hearing loss. Although ENT symptoms are not diagnostic of a disease, it might be suggestive of HIV infection or related to its progression and treatment efficacy. A better knowledge about the regional prevalence of ENT manifestation in HIV/AIDS patients help ENT surgeons, for better understanding and a multidisciplinary approach in treatment to these patients, as creation of awareness is the key to prevention.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Shanmuga AS, Rajendran S. A study on otorhinolaryngologic manifestations in human immunodeficiency virus infected patients. *Int J Otorhinolaryngol Head Neck Surg* 2020;6:471-7.