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Original Article

Ear,Nose and Throat Section

Otorhinolaryngological Manifestations among HIV Positive Children in Coastal Karnataka

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ABSTRACT

Introduction: With changed clinical profile of HIV related diseases, our study attempted to analyse otorhinolaryngological manifestations in HIV positive children coming to ART centre of a tertiary referral in South India.

Materials and Methods: Records of 137 children registered at ART Centre, Government Wenlock Hospital, Kasturba Medical College, Mangalore from 2004 till 2010 were studied and data for this retrospective study was collected.

Results: Twenty three (16.8%) children developed otorhinolaryngological manifestations, which were upper respiratory tract infection (13.1%), oral candidiasis (1.4%), otitis media (1.4%) and parotitis (1%). With increasing WHO stage, the ENT manifestations increased ($p<0.05$) while CD4 count decreased ($p>0.05$), 35% and 44% cases with ENT manifestations had CD4 counts above 500 cells/mm^3 and below 200 cells/mm^3 respectively ($p>0.05$). 24% children on HAART and 10.7% not on HAART developed ENT illnesses ($p<0.05$).

Conclusion: With the current ART protocols, ENT manifestations are seen in 17% HIV positive children, most of which are aspecific.

Keywords: AIDS, CD4 count, HAART, HIV, Otorhinolaryngology

INTRODUCTION

The incidence and prevalence of human immunodeficiency virus (HIV) infections are both raising to unexpected proportions the world over. The increasing number of peadiatric HIV infections is a matter of concern with increasing statistics being reported from poorer areas. However, in many parts of the world, better awareness of the disease and treatment of mother in antenatal and perinatal period along with early initiation of Highly Active Antiretroviral Therapy (HAART). In the HIV infected child has significantly changed the picture of peadiatric AIDS [1]. As in other systems, even in otorhinolaryngology, today many aspecific manifestations like sinusitis, otitis [1] etc are also seen rather than just the classical clinical manifestations of AIDS.

Our study records the otorhinolaryngological manifestations in paediatric HIV patients who are attached to our AIDS centre (also known as Antiretroviral Therapy (ART centre). It attempts to correlate the otorhinolaryngological manifestations with the severity of disease as judged by World Health Organization (WHO) staging and CD4 count of the patient. Moreover our study also highlights the variations in published literature regarding otorhinolaryngological manifestations from different parts of the world and attempts to analyse the reasons for the same.

MATERIALS AND METHODS

A retrospective study was done on 137 children who were registered and were being followed up at the Anti Retroviral Therapy Centre of our Government Wenlock Hospital, Mangalore from 2004 till 2010. After appropriate ethical clearance from the Institutional Ethical Committee, the records of these 137 children were analysed in the ART centre and the required information was noted down on a pretested proforma.

Inclusion Criteria

One hundred and thirty seven children who were registered at the ART centre of our hospital from the time of its inception in 2004 till 2010 were included in our study.

Exclusion Criteria

The exclusion criterion was non-availability of adequate data for the child.

Data Collection

The list of opportunistic infections/manifestations that the patient had was collated from the medical charts of the patient. The medical chart of each patient had a record of illnesses that the patient had from the time of first visit to the centre. The otorhinolaryngological manifestations included were upper respiratory tract infection, chronic suppurative otitis media, oral candidiasis and parotitis. Some of the other opportunistic manifestations that were included were pulmonary tuberculosis, lower respiratory tract infection, dermatitis, pneumonia, diarrhea, etc.

The medical chart of each patient had a record of illnesses that the patient had from the time of first visit to the centre . The illnesses were recorded by the physician at the ART centre on clinical examination of the patient but there was no evidence of historical data in the case sheets. The list of opportunistic infections that the patient had was collated from this data but repeated occurrence of the same illness was not taken into account. Hence our results do not include this data. The ART center was started in 2004 under the ART center scheme of Government of India. The children referred to the ART center were investigated for confirmation of diagnosis. CD4 count and WHO stage was done for each child. In the ART centre, the children were categorized into four stages of HIV at the time of registration as per WHO guidelines [2]. The CD4 count was done at registration and every six monthly thereafter.

Children were started on ART as per National AIDS Control Organization guidelines [3]. All children below the age of one year were put on HAART. Children above the age of one year with the CD4 count of <200/mm^3 were started on ART. Children with CD4 count between 200-349/mm^3 were started on ART if symptomatic. If CD4 count was more than 350/mm^3, ART was not started. The children on ART were seen every month when they were given the drugs while the children who were not on ART were expected to come every six months. For antiretroviral therapy, Highly Active Anti-Retroviral Therapy (HAART) was given as per NACO guidelines [4].

STATISTICAL ANALYSIS

The data was analysed using SPSS version 11.5. Association was found using chi square test and p-value<0.05 was taken as statistically significant.

RESULTS

Case records of HIV infected children who visited the ART Centre, Government Wenlock Hospital, Mangalore from 2004 till 2010 were included in the study. Few of these children were on their first visit while the others were on their three monthly follow-ups as required by the centre. There were 137 children in this group with age range of 0-12 year. Fifteen percent children came to this centre for the first time in the past one year, 22.6% had been coming here for 1-2 year, 26.3% for 2-3 year, 25.5% for 3-4 year and 10.3% for 4-5 year.

The study population consisted of 75 (54.7%) males and 62 (45.3%) females. The mean age was 7.55 years with a standard deviation of 2.98 year. 134 (97.8%) children were delivered by vaginal birth and the remaining three (2.2%) were born by Caesarean Section. Mothers of all the 137 children were infected by HIV. Only one child's father was not infected while the remaining 136 children's fathers were also infected.

Opportunistic Infections

It was observed that among the 137 children who were diagnosed to have HIV infection, 69 (50.4%) children presented with some form of opportunistic manifestations. Fourteen (10.3%) of 137 children developed otorhinolaryngological manifestations [Table/Fig-1], 46 (33.5%) children developed other systemic opportunistic manifestations and 19 (6.5%) children presented with both otorhinolaryngological and systemic manifestations.

Opportunistic manifestation	n (%)
Upper Respiratory Tract Infection	18 (13.1)
Chronic Suppurative Otitis Media	2 (1.4)
Candidiasis	2 (1.4)
Parotitis	1 (1)
Pulmonary Tuberculosis	18 (13.1)
Lower Respiratory Tract Infections	13 (9.4)
Diarrhoea	10 (7.2)
Dermatitis	9 (6.5)
Pneumonia	7 (5.1)
Herpes zoster	5 (3.6)
Others	7 (5.1)

[Table/Fig-1]: Profile of opportunistic manifestations among peadiatric HIV patients (N=137)

WHO Stage of Disease

WHO staging of the children at the time of registration at this ART centre was recorded. Among 137 children, 40 (29.1%) were in Stage I of HIV infection, 55 (40.1%) were in Stage II, 35 (25.5%) were in Stage III and seven (5.3%) were in Stage IV. [Table/Fig-2] shows the opportunistic manifestations in children with respect to WHO stage. Three percent of the children in WHO stage I developed opportunistic manifestations whereas 61.8% children in Stage II, 80 % children in stage III and 85.7% children in stage IV developed opportunistic manifestations. This was found to be statistically significant (p<0.001). All otorhinolaryngological manifestations were present either in stage II or stage III. In stage II, the ENT manifestations seen were Upper Respiratory Tract Infection (URTI) and Chronic Suppurative Otitis Media (CSOM). In stage III, Candidiasis and Parotitis were seen.

CD4 Count

[Table/Fig-2] shows development of opportunistic manifestations with respect to CD4 count. 66.7% children with CD4 count less than 200/mm^3 developed opportunistic manifestations, ten of whom developed otorhinolaryngological manifestations, which were URTI and candidiasis. In the CD4 count range 200-349/mm^3, 62.4% children developed opportunistic manifestations out of which four had otorhinolaryngological manifestation that was URTI. Forty four percent of the children with CD4 count more than 500/mm^3 developed opportunistic manifestations out of which eight children developed otorhinolaryngological manifestations, which were URTI, CSOM and parotitis. The relationship of CD4 count and opportunistic manifestations was not found to be statistically significant (p=0.09).

	No manifestations	ENT manifestations	Other manifestations
WHO Stage			
I	39 (97.5%)	1 (2.5%)	1 (2.5%)
II	21 (38.2%)	15 (7.3%)	22 (40%)
III	7 (20.0%)	7 (20%)	26 (74.3%)
IV	1 (14.3%)	0 (0%)	6 (85.7%)
χ^2=71.75, p<0.001			
CD4 count (/mm^3)			
0-200	10 (33.3%)	10 (33.3%)	15 (50%)
200-349	9 (37.6%)	4 (16.6%)	13 (54.1 %)
350-499	10 (71.4%)	1 (7.2%)	3 (21.4%)
>500	39 (56.5%)	8 (11.7%)	24 (34.9%)
χ^2=14.76, p=0.098			
Outcome			
Not on ART	47 (72.3%)	6 (9.2%)	13 (20%)
On ART	18 (29.5%)	12 (19.4%)	36 (60%)
Total	68 (49.6%)	23 (16.8)	55 (40.2)
χ^2= 33.88, p<0.001			

[Table/Fig-2]: Opportunistic manifestations as per WHO stage, immunological categories and treatment
Some patients had both ENT and other manifestations, hence the total number for the table is more than the sample size

Antiretroviral Therapy

Of the 137 children, 72 (52.6%) children were on anti retroviral therapy and 65 (47.4%) children have not yet been started on ART. The immunological categories and WHO staging who received HAART treatment at the ART centre is as shown in [Table/Fig-3].

	on ART	Not on ART
CD4 count (/mm^3)		
<200	30 (21.8%)	0
200-349	20 (14.5%)	4 (2.9%)
350-499	3 (2.1%)	11 (8%)
>500	19 (13.8%)	50 (36.4%)
χ^2 = 73.212, p<0.001		
WHO Stage		
I	3 (2.1%)	37 (27%)
II	32 (23.3%)	23 (16.7%)
III	31 (22.6%)	4 (2.9%)
IV	6 (4.3%)	1 (0.1%)
χ^2 = 57.312, p<0.001		

[Table/Fig-3]: Treatment status as per immunological categories and WHO stage

[Table/Fig-2] shows development of opportunistic manifestations with respect to treatment. 27.7% children who were not on anti-retroviral therapy developed opportunistic manifestations. 70.5% children currently taking anti-retroviral therapy developed opportunistic manifestations and 19.7% of them had otorhinolaryngological manifestations. (p<0.001).

Mortality

Eleven (8%) children died during the treatment. All of them were on ART. Among them, eight had developed opportunistic manifestations

of which five had developed otorhinolaryngological manifestations, which were URTI and candidiasis. Among these, four children were in Stage III and one child was in stage I. Also, four children had CD4 count below 200/mm^3 while one child had CD4 count in the range of 200- 349/mm^3.

DISCUSSION

The incidence and prevalence of adult HIV infections are increasing the world over. This is associated with an increase in pediatric HIV infections. In infants and children, 15-20% develop an AIDS defining illness by one year and the median age of progression to clinical AIDS is approximately six years [5]. Fifty five percent of HIV children present with their first otorhinolaryngological disease before the age of three years and 98% before the age of nine years [1].

Otorhinolaryngological disorders already common in pediatric population are more frequent in HIV population since the upper airway is the natural interface between the organism and environment [1]. According to WHO staging of clinical disease for children below 15 y of age, the otorhinolaryngological manifestations of persistent generalized lymphadenopathy is in stage I, recurrent upper respiratory infections, recurrent oral ulcerations and parotitis is in Stage II, oral candidiasis and oral hairy leukoplakia is in stage III while extrapulmonary tuberculosis, oesophageal candidiasis and malignancies are in stage IV [2].

In the 137 children in our study, otorhinolaryngological manifestations were recorded in 16.8%. Otorhinolaryngological manifestations were recorded in 91% children from UK [6] and 100% children from Brazil [7]. A study from a TB and HIV referral centre in Chennai, India [8] reported almost a 70% incidence of head and neck manifestations. We attempted to analyse the reasons for the low incidence of otolaryngological manifestations. It is known that HAART improves the control of immunodeficiency with reduced incidence of ENT manifestations like oral candidiasis, tumours and parotid cysts. [1] 1.4% of our patients had oral candidiasis but we had no tumours or parotid cysts. Thus the reduced ENT manifestations could be attributed to timely treatment with HAART. However, our study was solely done from records from the ART centre. The patients are examined by the medical officer in the ART centre and if deemed relevant patients are sending to the speciality outpatient departments for consultation. In this scenario it is possible that some of the aspecific infections of HIV could be considered irrelevant and not captured in the case records. Moreover in our ART centre, the patients were not required to maintain a symptom diary, so some of the opportunistic infections, which developed in between the follow-ups, might have been missed.

The manifestations reported in literature in the nose and paranasal sinuses in relation to HIV are recurrent rhinitis, sinusitis, nasal vestibulitis, epistaxis, hyposmia and hypoguesia [1,9,10]. Sinusitis, though not reported in many studies including ours, has a close association with the immunodeficiency of AIDS. All of these do not find a mention in many paediatric HIV reports. In the duration of one year, 13.1% children in our study have been recorded to have recurrent URTI. There is no mention of tonsillar or throat infection in our records. Figures in reports across the world vary with no mention as in Nigeria [11], to 7.8% as reported in Chennai, India [8] to as high as 34.5% in Thailand [9] for rhinitis and 0.8% for sinusitis. WHO guidelines include tonsillitis, adenoiditis, otitis media and pharyngitis under the broad heading of upper respiratory infections but no clear definition is present regarding transition from a common childhood URTI to an AIDS defining rhinosinusitis.

The incidence of otitis media in children is known to vary from 18-36% [1]. Early reports from the eighties reported that eight out of ten peadiatric cases had conductive loss because of otitis media [12]. Otitis media with otorrhoea was noted in 18% of cases from a pediatric study in Thailand [9] with no reference to acute otitis media in records, while a further cross sectional study in search of acute suppurative otitis media revealed 28% cases of acute infection. Forty four percent of HIV infected children had purulent otitis media either with an intact drum or frank otorrhoea in a study where a paediatric otolaryngologist or an infectious disease specialist saw all cases [6]. They have conceded that their actual numbers of acute infections may have been higher since some of the children might have been treated at a primary level [6]. Reports of a large study from a HIV and TB referral centre in India [8] do not say otitis media while our study showed an incidence of only 1.4%.

Oral candidiasis is the most common mucocutaneous manifestation of AIDS in the pediatric population and is reported in 65-70% of symptomatic cases in some centres [13]. Oral candidiasis represents progressive disease with poor prognosis in children more than six months [14] and falls into stage III of disease [2]. The incidence of the disease again shows variation in numerous studies- 90% in Nigeria [12], 60% in Thailand [10], and 20% in Romania [15]. Our study showed only a low incidence of 1.4%. A study from North Eastern India from an otolaryngology department showed an incidence of 22.5% in their referred HIV cases [16] and another study from a TB and HIV referral centre showed an incidence of 36.4 % [8].

The presence of persistent generalized lymphadenopathy makes the patient a stage I disease while TB lymphadenopathy pushes the patient into stage IV [2]. Cervical lymphadenopathy in children varies from 40-70% [1]. However, reports of incidences of TB lymphadenopathy varies. Paediatric reports from a TB and HIV referral centre show the incidence to be about 23% [8]. A report from Nigeria reported 58% of lymphadenopathy but only one case of TB lymphadenitis [11]. Our report does not give any incidence of cervical/generalized/tuberculous lymphadenopathy being recorded at our centre.

Bilateral parotid swelling is a classical feature of AIDS. They are seen in children who are termed as slow progressors who after several years may have decline in the CD4 count and allow a more classical picture of AIDS to appear [7]. However, the incidence in studies varies from 5% [1] to 30% [13].

When we considered all opportunistic infections, the majority (85.7%) developed in stage IV of disease (n=7), while compared to stage I (2.5%) but when we consider otorhinolaryngological manifestations alone (27.2%), they were most common in stage II of the disease (n=55). This was found statistically significant. When otorhinolaryngological manifestations were compared to CD4 counts, the incidence of otorhinolaryngological disease was seen to increase with decreasing CD4 count. This was not found statistically significant. Our study seems to suggest that with the current treatment protocol, most of the otorhinolaryngological manifestations are in stage II of WHO stage of disease.

Of the children who were on ART, 23.6% developed otorhinolaryngological manifestations while 58.3% developed non otorhinolaryngological other systemic manifestations. 9.2% patients who were not on ART developed otorhinolaryngological manifestations as against 20% who developed other systemic manifestations. The results were statistically significant. The results show that HAART does not prevent otorhinolaryngological or other systemic manifestations from occurring in patients with low CD4 counts. HAART has been seen to significantly reduce otorhinolaryngological manifestations and improve CD4 count while compared to ART (mono-drug regimen) [1]. The change from ART to HAART has been seen to drastically reduce otorhinolaryngological manifestations including oropharyngeal candidiasis by two-thirds while it completely prevents the occurrence of diseases like benign lymphoepithelial parotid cysts and head and neck tumours [1]. In our centre where HAART is prescribed according to age and CD4 counts, no cases of malignancy or extrapulmonary tuberculosis and only very few cases of oral candidiasis and parotitis have been reported.

Our study has recorded very low incidence of some of the otorhinolaryngological manifestations when compared to some other studies [8,17]. In our own institution a study was published with data collected from 1996-2004. This study of 968 patients was done mainly in the adult population. The study group comprised of patients who had come to the hospital from 1996 onwards; a time when the national AIDS control programme in India was in its infancy. Since the ART centre was not functional at the time (the ART centre opened only in 2004) the patients directly came with ear, nose and throat complaints to the department or were sent to the department with a diagnosis of HIV from other wards. In contrast the present study comprised of children on follow up at the ART centre which started in 2004 in our hospital. In the ART centre depending on the CD4 counts, the children are started on HAART which is known to reduce the ENT related manifestations of AIDS.

The wide variation in incidences of paediatric otorhinolaryngological diseases that we see in literature is worth noting. Some of the variations are accounted for by the decade in which the reports have been published [1,8,9,12]. Studies reported from Otolaryngology or Dental departments note otorhinolaryngological manifestations in detail whereas a general AIDS referral centre is unlikely to report all otorhinolaryngological diseases in detail. Retrospective studies have to depend on the data provided by case records, while in prospective studies even trivial complaints can be recorded since direct questioning and examination of the patient do the compilation of data. Since these records reflect the progression of disease in a country they may be a guide for future Government initiatives.

This study offers a glimpse of otorhinolaryngological manifestations in paediatric HIV patients recorded in an ART centre in India. Manifestations like upper respiratory tract infection and otitis media are the most frequent otorhinolaryngological manifestations in this study. The fact that an otolaryngologist commonly treats such aspecific diseases in the general population can lead to delay in diagnosis. In an undiagnosed patient only an otolaryngologist with a high index of suspicion can order for appropriate tests.

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