



# Hearing Disorders among HIV Positive Children at the University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria

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## Authors' contributions

*This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.*

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## ABSTRACT

**Background:** Use of antiretroviral drugs (ART) has changed the epidemiology of HIV disease, making it a chronic illness and with many people developing long term sequelae of the disease such as hearing loss. This study compared hearing disorders, its types and severity among children with and without HIV disease.

**Methods:** This was a hospital based comparative cross-sectional study carried out among eligible patients who were HIV positive, aged 6 to 15 years recruited via systematic sampling method and matched by age and sex with HIV negative controls. An interviewer-administered questionnaire was used to extract the sociodemographic characteristics of the subjects, patients/caregivers awareness of hearing impairment and to document the otoscopic, Pure tone audiometry (PTA) and tympanometry findings performed on the patients. CD4 count was done for all the study participants while all HIV positive patients were graded for severity using WHO clinical Staging.

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Obtained data was analysed using the statistical package for social sciences (SPSS) version 22. A p-value of less than 0.05 was considered statistically significant.

**Results:** A total of 400 children aged 6 years to 15 years were recruited for the study out of which 200 were HIV positive (cases), while 200 were HIV negative (controls). Otitis media with effusion, otitis media and perforated tympanic membrane were the predominant tympanometry and otoscopic findings. Seventy-three (36.5%) of the HIV positive patients had hearing loss compared to 19(9.5%) of HIV negative patients and this was statistically significant ( $X^2 = 41.1$ ;  $p = 0.0001$ ). Majority (95.9%) of persons with hearing loss had the conductive type and of mild degree 53 (72.6%). Only 3(4.1%) caregivers of the HIV positive children and 1 (5.6%) caregiver of the HIV negative children were aware of the hearing impairment in their children but none had complained to their primary health caregivers.

**Conclusion:** This study has established a higher rate of hearing loss, of the conductive type and of mild degree among HIV positive patient. It is necessary to assess and monitor the hearing in HIV positive children by conducting interval PTA testing and Tympanometry to ensure timely intervention since parental awareness is poor.

*Keywords: Hearing disorders; HIV positive children; antiretroviral drugs; HIV disease.*

## 1. INTRODUCTION

HIV has remained a global problem with an estimated 1.8 million children less than 15 years of age being affected [1]. Study show that about 80% of patients with HIV infection present with otolaryngological symptoms [2,3]. The advent, availability and use of potent Highly anti retroviral treatment (HAART) in many low-income countries in the past decade is changing the natural history of the disease with many long-term survivors [4]. With this in view, there is increasing life expectancy among people living with HIV and the disease is fast becoming a chronic illness, therefore, emphasis on improving the quality of life rather than saving life must be pursued [5]. Evidence show that with increasing life expectancy, long term consequences of the disease become evident and hearing impairment is a potential long-term consequence of HIV disease [6].

Hearing loss in HIV is usually gradual in onset but can be sudden as well and studies have shown that sensorineural hearing loss represents about a third of hearing loss in adults and this may result from opportunistic CNS infections causing encephalitis, meningitis (Toxoplasmosis, CMV, Herpes, syphilis) or from HIV virus itself [7-10]. It may also be iatrogenic, from the ototoxic effects of medications used in treatment of opportunistic infections like Tuberculosis, acute respiratory disease. Since sensorineural hearing loss is irreversible, emphasis should be on prevention rather than treatment [8,10]. Hearing loss also occur in children with HIV and study show that it is mainly conductive hearing loss (i.e. mainly located in the middle ear) probably

because immunocompromised children are at increased risk of developing otitis media and chronic suppurative otitis media [11,12]. Otitis media with effusion (OME) secondary to nasopharyngeal lymphoid hyperplasia or other nasopharyngeal masses has also been implicated [13]. Otitis media with effusion causing a conductive hearing loss, frequently follow obstruction of the Eustachian tubes by lymphoid mass in the postnasal space [13]. These conditions frequently affect Paediatric patients with HIV disease because Eustachian tube dysfunction typical of this age group combined with depressed cell-mediated immunity markedly increases their susceptibility to ear infection [13]. This means that in children, hearing loss is treatable if facilities are available for early detection.

Hearing is measured in decibels and depending on the decibels lost, the degree of hearing loss can be classified into mild, moderate and severe. Other classifications are; slight, mild, moderate, moderately severe, severe and profound [14]. These degrees of hearing loss are progressive and most children with severe and profound hearing loss can only function with a cochlear implant with or without a hearing aid, so early detection is imperative in management since treatable causes are common in children.

Though there is paucity of ENT surgeons in many low-income countries, early assessment and detection of hearing loss in children with HIV is important as hearing is necessary for social interaction and child education. It will also help to show how best to prevent or treat patients with hearing impairments. This study was carried out

to determine the prevalence, type and degree of hearing loss among children aged 6-15 years with HIV on HAART in UPTH and to compare the hearing loss between HIV positive patients with age and sex matched HIV negative controls.

## 2. METHODOLOGY

This was a hospital based comparative cross-sectional study carried out over a nine month period among 200 HIV positive and 200 HIV negative children receiving care at the consultant Paediatric HIV clinic and children outpatient clinic of the University of Port Harcourt Teaching Hospital (UPTH) respectively. Ethical approval for the study was obtained from the University of Port Harcourt Teaching Hospital Research and Ethics Committee. Written informed consent was obtained from the parents/guardian of these children while Assent for children more than 7years were obtained before inclusion into the study. Anonymity and confidentiality were maintained in the study. The sample size was calculated using the formula for cross sectional studies [15]  $n = \frac{z^2 pq}{d^2}$  Where: n=the minimum sample size, Z=the standard normal deviation, usually set at 1.96, which corresponds to the 95% confidence level, p = the proportion in the target population estimated to have a particular characteristic. Prevalence of hearing disorder was 8.8% among HIV positive children aged between 6 and 12 years in a similar study by Nukku et al. [16].

$$q = 1 - p$$

d = desired degree of accuracy, set at 0.05.

$$n = \frac{(1.96)^2(0.088)(0.912)}{(0.05)^2} = \frac{(3.8416)(0.0803)}{0.0025}$$

$$= 123.392 \text{ approximated to } 124$$

Allowance for 20% non-response = 124 + 24 = 148. This was rounded up to 200 to improve the validity of the study. The study therefore, comprised of 200 HIV positive Paediatric patients and 200 HIV negative controls, making a total sample size of 400.

Eligible patients who were HIV positive and aged 6 to 15years were recruited via systematic sampling method and matched by age and sex with controls (HIV negative children). Hospital records shows that, an average of 40 HIV

positive children aged between 6years to 15years are seen on weekly basis. In order to attain the sample size, 10 patients were sampled on each clinic day using a calculated sample interval of four. The first sample was selected by a simple random sampling via balloting, after which every 4<sup>th</sup> patient was selected in line with the sampling interval. Patients whose parents declined consent were replaced by the next available patient until the total sample size was obtained.

The lower age of 6 years was taken because Pure Tone Audiometry (PTA) is conducted on children old enough to cooperate with the test procedure. An interviewer-administered questionnaire in English language was used to extract data from the participants and to document findings of otological and hearing assessment carried out on them. The questionnaire comprised of three sections: Section A contains information on socio-demographic characteristics of the participants and patients/caregivers awareness of hearing impairment; Section B was used to capture data on the HIV status, CD4 count and WHO clinical staging of the subjects while section C of the questionnaire was used to document findings of otoscopy, tympanometry, PTA and hearing assessment of the subjects. All patients had an otoscopy, PTA and tympanometry performed on them by an ENT surgeon for diagnosis of hearing loss and its characteristics. Otoscopy was done for each ear using a standard Otoscope for ear examination (Battery operated ACC133M Heine Mini 3000 Otoscope, Germany) and a disposable speculum. PTA was carried out using Madsen, Itera model, serial number 211150, Denmark. Manufacture date 11/2004(accuracy  $\pm$  1%), calibrated 1<sup>st</sup> December 2018( calibrated yearly) in a sound proof booth (Kahntact BB 100 model, made in USA), after the audiometric procedure was explained to the subjects, with emphasis on the type of sound that will be generated by the audiometer, and how the subjects should respond when the sound is heard. Both ears were tested separately for both Air and Bone conduction. Pure tone audiometric threshold were determined using 250HZ, 500HZ, 1000HZ, 2000HZ, 4000HZ, 8000HZ for both air and bone conduction. The pure tone audiograph was then obtained for analysis. Tympanometry was done on both ears using a tympanometer, Madsen, Zodiac 901 model, serial number 217384, Denmark. Manufacture date 03/2005(accuracy  $\pm$ 5%), calibrated 16<sup>th</sup> April 2018. (calibrated yearly).

HIV positive patients were graded for severity using WHO clinical Staging (stages 1, 11, 111 and 1V). The WHO clinical staging of the HIV positive subjects was determined using the documented current clinical staging in the case notes of the subjects and confirmed with the WHO clinical staging of HIV disease in children [17]. They were classified as Stages I, II, III and IV. CD4 count for all the study participants were determined. CD4 count was done using venous blood that was drawn from the forearm of all subjects and the controls using a 2 ml syringe. into a pre-labelled EDTA bottle and sent to the laboratory for analysis. HIV testing for the controls were done using 0.5ml of venous blood withdrawn from the EDTA bottle using a precision pipette and transferred to the rapid diagnostic test (RDT) kit, then a drop of buffer solution was added into the kit. The timer was placed at 15minutes when the results were read in accordance with the recommended HIV serial testing by the National Guidelines on HIV counselling and testing using the Rapid Diagnostic Kit to ascertain that the controls do not have HIV. Obtained data was analysed using the statistical package for social sciences (SPSS) version 22. Descriptive statistics were used to describe socio-demographic characteristics of the participants. Chi-square statistics and Fischer's exact test were used to compare the differences in proportions while independent t-test was employed to compare the differences in means across the groups. A p-value of less than 0.05 was considered statistically significant.

### 3. RESULTS

#### 3.1 Socio-demographic Characteristics of Study Participants

A total of 400 children aged 6 years to 15 years were recruited for the study out of which 200 were HIV positive (cases), while 200 were HIV negative (controls). The mean age was  $10.18 \pm 3.04$  years for the HIV positive children and  $10.65 \pm 3.17$  years for the control group. ( $\chi^2 = -0.25$ ,  $p = 0.8807$ ). Females constituted 113 (56.5%) and 108 (54.0%) among the HIV positive and HIV negative cases respectively, with a male to female ratio of 1:1.3 and 1:2 among the HIV positive and negative cases respectively. Of the 200 HIV positive cases, 179 (89.5%) belonged to WHO clinical stage 2, 15 (7.5%) of them were in clinical state 3 and 6 (3.0%) were in clinical state 1. Table 1 shows that there was no statistically

significant difference between the proportions of the age and sex categories of the study participants across their HIV status ( $p = 0.8807$  and  $p = 0.8813$ ).

#### 3.2 Otosopic Findings among HIV Positive and HIV Negative Study Participants

Sixteen (8.0%) and 11 (5.5%) of the HIV positive patients had perforated tympanic membrane and otitis media respectively. There was no statistically significant relationship in the otoscopic findings between the HIV positive and negative patients. (Table 2).

#### 3.3 Tympanometry Findings among HIV Positive and HIV Negative Study Participants

Type B - Otitis media with Effusion (OME) was found in 83 (41.5%) of the HIV positive patients and was the most common abnormal pattern noticed on tympanometry. There was a significantly higher rate of Type B abnormality among those who were HIV positive in comparison to those who were not ( $p = 0.0001$ ). Table 3.

#### 3.4 Prevalence of Hearing Loss among HIV Positive and HIV Negative Study Participants

Table 4 shows that 73 (36.5%) of the HIV positive patients had hearing loss compared to 19(9.5%) of HIV negative patients. The overall hearing loss was 23.0%. There was a statistically significant difference between hearing loss and the HIV status of the patients. ( $\chi^2 = 41.1$ ;  $p = 0.0001$ ).

#### 3.5 Distribution of Type of Hearing Loss and Degree of Hearing Loss among HIV Positive and HIV Negative Participants

Majority of persons with hearing loss 70(95.9%) had the conductive type and of mild degree 53 (72.6%) among the HIV positive patients. The degree of hearing loss in decibels for the mild, moderate and severe forms are stated in parenthesis in Table 5. The differences in the proportions of the type of hearing loss and degree of hearing loss were not statistically significant across the HIV positive and negative persons ( $p = 0.6822$  and  $p = 0.6983$ ).

**Table 1. Socio-demographic characteristics of study participants**

Variables	HIV Positive n(%)	HIV negative n(%)	Total n (%)	Chi- Square	p-value
<b>Age group</b>					
6-10years	110 (55.0)	115(57.5)	225(55.8)	0.25	0.8807
11-15 years	90(45.0)	85(42.5)	175(44.2)		
<b>Sex</b>					
Males	87(43.5)	92(46.0)	179(44.6)	0.25	0.8813
Females	113(56.5)	108(54.0)	221(55.4)		
<b>Total</b>	<b>200(100%)</b>	<b>200(100%)</b>	<b>400(100%)</b>		

**Table 2. Otosopic findings among HIV positive and HIV negative study participants**

Variables	HIV Positive n (%)	HIV Negative n(%)	Total n (%)	Fischer's exact
Perforated TM	16(8.0)	6(3.0)	22(5.5)	2.15
Otitis media	11(5.5)	2(1.0)	13(3.3)	(0.3142)
Otomycoses	5(2.5)	0(0.0)	5(1.3)	

**Table 3. Tympanometry findings among HIV positive and HIV negative study participants**

Tympanometry findings	HIV Positive n (%)	HIV negative n (%)	Total n (%)	p-value /Fisher's exact
Type A (Normal)	116 (58.0)	180 (90.0)	296 (74.0)	53.99
Type B (OME)	83 (41.5)	19 (9.5)	102(25.5)	53.99 (0.0001)*
Type C (ETD)	1 (0.5)	1 (0.5)	2 (1.0)	0.6318
<b>Total</b>	<b>200 (100.0)</b>	<b>200 (100.0)</b>	<b>400 (100.0)</b>	

\*Statistically significant

OME: Otitis media with effusion

ETD: Eustachian Tube Dysfunction

**Table 4. Prevalence of hearing loss among HIV positive and HIV negative study participants**

Hearing loss	HIV Positive n(%)	HIV Negative N (%)	Total n (%)	Chi-square	p-value
Present	73 (36.5)	19 (9.5)	92 (23.0)	41.1	0.0001*
Absent	127 (63.5)	181 (90.5)	203 (77.0)		
<b>Total</b>	<b>200 (100.0)</b>	<b>200 (100.0)</b>	<b>400 (100.0)</b>		

\*Statistically significant

**Table 5. Type and degree of hearing loss among HIV positive and negative study participants**

Variables (N=57)	HIV Positive n (%)	HIV negative n (%)	Total n (%)	Fisher's exact p-value
<b>Type of hearing loss</b>				
Conductive	70(95.9)	18 (100.0)	88 (96.7)	0.76 (0.6822)
Sensorineural	3 (4.1)	0 (0.0)	3 (3.3)	
<b>Degree of hearing loss</b>				
Mild (26-40dB HL)	53 (72.6)	16 (88.9)	69 (75.8)	2.20 (0.6983)
Moderate (41-55dB HL)	18 (24.7)	2 (11.1)	20 (22.0)	
Severe (56-90dB HL)	2 (2.7)	0 (0.0)	2 (2.5)	

dB- Decibels

HL- Hearing Loss

**Table 6. Comparison of mean CD4 count by hearing loss status among HIV positive study participants**

Variable	Hearing loss Mean ± SD	No hearing loss Mean ± SD	T	p-value
CD4 count	682.15±409.09	851.93±476.24	-2.040	0.043*

\*Statistically significant

### **3.6 Caregiver Awareness of Hearing Impairment**

Only 3(4.1%) caregivers of the HIV positive children and 1 (5.6%) caregiver of the HIV negative children admitted to a prior history of hearing impairment in their children but none had complained to their primary health caregivers.

### **3.7 Relationship between CD4 Count and Hearing Loss among HIV Positive Patients**

Table 6 shows that the mean CD4 count was significantly lower in HIV positive patients with hearing loss than the mean CD4 count in HIV negative patients ( $p=0.043$ ).

## **4. DISCUSSION**

In this study, perforated tympanic membrane and otitis media were the commonest otoscopic finding while OME was the commonest abnormality on tympanometry and these were contributed to mainly by HIV positive patients. These findings have been shown by various authors [12,13] and is said to significantly contribute to hearing loss and ETD among children with severe HIV disease. However, in this study very few patients had ETD and this may stem from the fact that many HIV patients in this study population were well controlled on HAART and belonged to WHO clinical stage 2 which indicates an early disease stage or good response to HAART.

The overall prevalence of hearing loss found in this study was high (23.0%) and this agrees with the report of previous authors [14,18]. Additionally, the rate of hearing loss was significantly higher among children with HIV (36.5%) in comparison to those without HIV (9.5%). This falls within the reported range of 14-49% documented from previous studies among HIV positive patients [19-22]. Otitis media is a common implicated aetiology in HIV positive patients and so is otitis media with effusion and both occurred in a larger proportion of HIV positive patients in this study. The effects of secondary opportunistic infections which are prevalent in HIV patients, ototoxic drugs, or the virus directly affecting the central nervous system, peripheral nerves, vestibulocochlear nerve or the cochlea cannot be undermined. [23,24].

Majority of children with hearing loss in this study had the conductive type of hearing loss as diagnosed by pure tone audiometry (PTA). Other authors have also reported similar pattern of hearing loss, [25-28] though sensorineural hearing loss [29-31] or central auditory disorders [32] have been reported in some series as the predominant type of hearing loss in HIV infected children. The high prevalence of conductive hearing loss in this and other studies was likely due to high rates of ear infections and middle ear abnormalities, such as Otitis media and perforated tympanic membranes that are associated with immunocompromised status in HIV positive patients, [13,32-36] Conductive hearing loss could also result from otitis media with effusion, this may occur following obstruction of the Eustachian tubes by lymphoid mass in the post nasal space as was observed in this study where 83 (41.5%) were found with OME.

Due to limited research in this area, the actual mechanism for sensorineural hearing loss (SNHL) in children with HIV is not known, but mitochondrial disorders are known to be associated with SNHL [37,38] and HIV and its treatment are associated with mitochondrial dysfunction, building a plausible mechanism for increased SNHL risk in HIV infected children. Mitochondrial abnormality is a risk factor for non syndromic sensorineural hearing loss associated, for example, with the A1555G mutation, [37,39] and this mutation has also been shown to predispose for sensorineural hearing loss after aminoglycoside use [38,40]. The direct effect of HIV on the cochlea has been established in a study by Pappas et al. [41] who identified extracellular viral-like particles in the tectorial membrane of three HIV positive patients with sensorineural hearing loss. They also identified pathologic changes in the labyrinthine wall, epithelial lining of macula and crista, and inclusion bodies in the supporting cells. Also, these children could also have SNHL on the basis of an undetected genetic, or congenital abnormality, neurologic disorder, or damage from congenital infection (e.g., cytomegalovirus [CMV]) or ototoxic drug exposure.

There was no significant relationship found between the degree of hearing loss and the HIV status. Hence it could be deduced that although hearing loss is associated with HIV positivity, this may not affect the degree of hearing loss. This finding may have arisen from the fact that the HIV children in this study were mostly stabilised

on their antiretroviral medications as shown in their WHO clinical staging.

Though majority of the hearing defect was of mild degree, it is surprising that only 4.1% of caregivers of the HIV positive children and 5.5% of the HIV negative children were aware of the hearing defect in their children and none of them had mentioned to their primary physicians. This may be due to the fact that less than 2% of them had severe hearing loss or to poor interpersonal skills of the health care givers which discourages openness between patients and healthcare providers. It also confirms the gradual onset nature of hearing defect in majority of individuals but emphasises the importance of early screening and detection of hearing disorder in children generally but especially among HIV positive patients, knowing the fact that the aetiology of most conductive hearing disorder in children with HIV is reversible when detected early.

Though many of the study participants who were HIV positive were stable at the time of data collection, there was a significantly lower CD4 count among HIV positive patients with hearing loss in comparison to those without hearing loss. CD4 count level is a measure of the immunological competence of an individual with lower levels signifying lower immunity. Torre et al. [21] also found an increased incidence of hearing impairment and other disorders being commoner in children with lower CD4 count levels and higher WHO clinical staging as was found in this study. Ascertaining the WHO clinical staging of these children at the time of HIV diagnosis rather than at the time of data collection may have shown clarity to the degree of immunosuppression in these children, this is because the degree of immunosuppression determines the risks of opportunistic infections in these children. This may have given better clarity to the observed high prevalence rate of hearing loss in these children in relation to the WHO clinical staging.

## 5. CONCLUSION

This study has established a higher rate of hearing loss of the conductive type and of mild degree among HIV positive patient. Otitis media, perforated tympanic membrane and OME were the common abnormal otoscopic and tympanometric findings elicited in this study. It is necessary to periodically assess and monitor the hearing in HIV positive children to ensure timely

intervention especially as parental awareness and reporting is low.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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