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THE PATTERN OF HEARING DISORDERS IN HIV POSITIVE PATIENTS ON ANTI - RETROVIRALS AT KENYATTA NATIONAL HOSPITAL

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THE PATTERN OF HEARING DISORDERS IN HIV POSITIVE PATIENTS ON ANTI - RETROVIRALS AT KENYATTA NATIONAL HOSPITAL

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ABSTRACT

Objectives: **To determine if patients on Anti - retroviral drugs (ARVs) develop hearing impairment.**
Design: **The comprehensive care clinic (CCC), Kenyatta National Hospital (KNH), Nairobi.**
Setting**: Case controlled study.**
Subjects: **Two hundred and seventy one human immunodeficiency virus (HIV) positive patients on ARVs were matched for age and sex with 273 HIV positive patients who were not on ARVs.**
Results: **Thirty four percent of HIV positive patients not on ARVs had a hearing loss compared to only 28% in patients who were on ARVs. sensorineural hearing loss was the most frequent hearing disorder in both groups. Majority of the patients had mild hearing loss and the higher frequencies were the most affected. There was a notable worsening of hearing loss with increase in age, but this was not statistically significant. It was noted that HIV positive patients hearing level worsened on starting ARVs but this improved after six months of ARV treatment.**
Conclusion: **Prolonged usage of ARVs is not associated with decreased hearing function. The most common hearing loss found in patients on ARVs is sensorineural hearing loss (SNHL).**

INTRODUCTION

Patients infected with HIV often present with derangements involving the ear, which negatively impact on the quality of life. The actual incidence of ear disease and hearing loss in this patient population is not known and this is of particular concern because the disability of partial or complete hearing loss is magnified in a person with many other medical problems (1).

A variety of adverse effects have been attributed to treatment with nucleoside reverse transcriptase inhibitors (NRTIs) but so far only a few cases ofneuro-ototoxicity have been reported in the literature (2,3). HIV infections together with opportunistic infections have been reported in literature to cause up to 50% of the hearing loss (4). Marra *et al*. showed that HIV-1 infected patients without significant immunosuppression developed hearing abnormalities during the follow-up particularly after exposure to anti - retroviral drugs (3, 4,). The hearing impairment is common with use of NRTIs, especially lamivudine, didanosine and stavudine and therefore patients on these drugs need to have close auditory function assessments during clinic visits to be able to pick out the impairment before they cause permanent damage. The patients with stable hearing impairment tend to deteriorate more rapidly after commencement of anti - retroviral therapy (1-3).

The goals of antiretroviral treatment are to improve the quality of life and reduce HIV related morbidity and mortality. However, this is undermined by the reports that some of the ARVs cause hearing loss thereby negating its very purpose.

This study was done to audiologically evaluate the patients who had been prescribed ARV drugs to establish if they were developing any significant hearing impairment compared to HIV infected patients who were not on ARVs.

MATERIALS AND METHODS.

This was a hospital based case control study done between November 2006 and April 2007 at

the comprehensive care clinic, Kenyatta national hospital. A minimum sample size of 271 was required in each arm. The study subjects were HIV positive patients aged 18 to 50 years who had been on anti - retroviral drugs for at least three months whereas the controls were HIV positive subjects not on ARVs because they were new diagnosis or the CD4 cell counts were above 350 cells per microlitre. All the patients were on the 1st line ARV drugs namely stavudine, efavirence and lamivudine (5). They were matched for age and sex. Patients who suffered diabetes, meningitis, head injury or cerebrovascular accident and those who had prior exposure to known ototoxic medications were excluded from the study. Subjects who satisfied the criteria were consequently recruited into the study after written informed consent. A clinical history was taken followed by thorough physical examination, otoscopy, tuning folk tests and PTA. All the audiological tests were performed by the same person. Data analysis was done using SPSS 10.0 software and descriptive statistics were done. Approval to carry out this study was obtained from the Ethics and Research committee of Kenyatta national hospital.

RESULTS

There were 271 study patients matched for age and sex against 273 controls, Figure 1 below. Most of the patients were in the age group 32 years to 38 years.

In the study group, 28% of the subjects had a hearing loss whereas in the control it was 34%. Hearing loss was more prevalent in patients who were not on ARVs than those who were already on treatment but this was not statistically significant (P=0.12). There was a general increase in the hearing loss with increasing age (Figure 2) but this was not statistically significant P =0.052. The hearing loss due to presbyacusis was not corrected since all the patients were below 50 years old.

Figure 1
Age Distribution

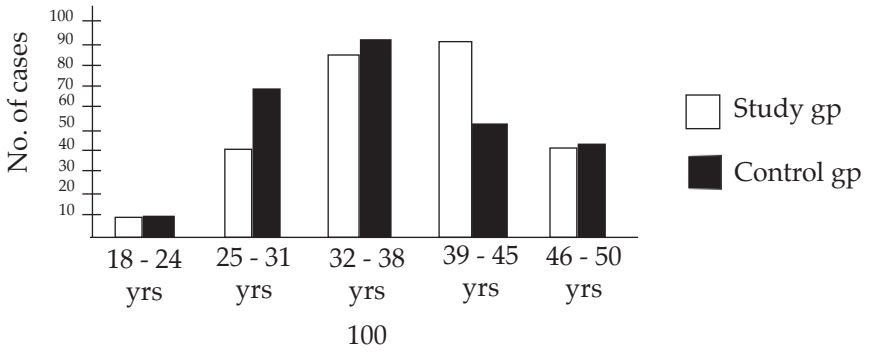
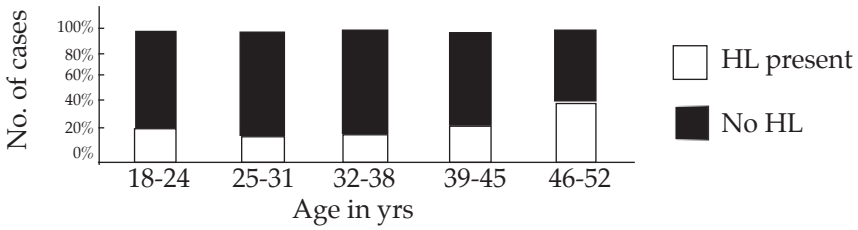


Figure 2
Age and hearing loss (HL)



Sensorineural hearing loss (SNHL) was the most common type of hearing loss in all age groups in both study and control groups followed by conductive hearing loss and a few patients had mixed type of hearing loss, Figure 3. In comparison, patients on ARVs had less CHL than those who were not on treatment Figure 3.

There was notable worsening of hearing level on initiation of ARVs which continued up to 6 months but thereafter there was a gradual improvement of hearing level (figure 4). However the trend improvement was not statistically significant (p=0.054).

Figure 3

Types of Hearing loss along the age groups in control and study groups

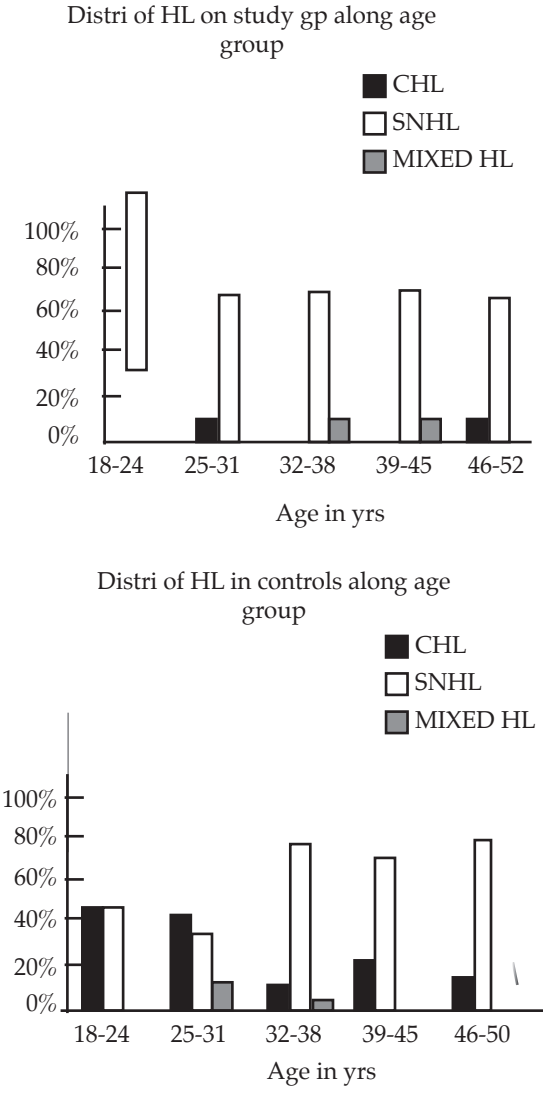
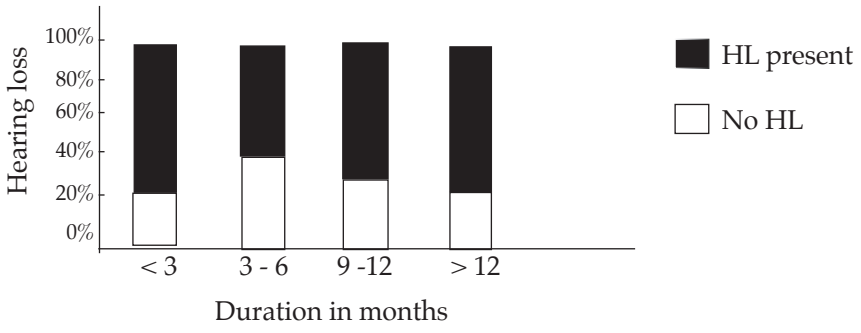


Figure 4

Duration of ART use and hearing loss



DISCUSSION

Twenty eight percent of patients on anti-retroviral therapy had a hearing loss of more than 25 dB in at least one of the hearing frequencies compared to 34% in the control group. Chandrasekhar *et al* in New York looked at 50 patients exposed to Zidovudine and Didanosine and found that 29% had a hearing loss (1). In this study there was no statistical difference in hearing loss between patients on ARVs and those who were not yet on ARVs (p=0.l2). However, some ARVs have been implicated in causing hearing loss (2, 6). In a prospective study done by Schouten *et al*, it was found that treatment with zidovudine and didanosine did not result in loss of hearing, even after taking into account noise exposure, immune status and age. The results of this prospective pilot study did not support the notion that treatment with nucleoside anti - retrovirals damages hearing (7).

In this study, patients who had been on ARVs for less than six months experienced worse hearing loss compared with those who had been on ARVs for more than six months. There was a general trend of worsening in the hearing level up to six months of treatment thereafter there was a general improvement in hearing level (Figure 4). This improvement in hearing could have been due to decrease in viral load and improved immunity and central nervous system functions at the retro-cochlear level. It can also be postulated that the initial hearing loss caused by ARV toxicity was cancelled out by the overall gains in improved immunity and reduced viral load. Rey *et al* reported patients who developed sensorineural hearing loss after exposure to ARV s, but improved several months later after stopping the ARVs (6). The control group could not be followed up to six months for ethical reasons as the desease progressed since most of them were started on ARVs.

There was notable general increase in hearing loss with advancement of age though this was not statistically significant p> 0.05 (0.052). Marra *et al* also found an interaction between age and anti - retroviral therapy which was significant (p = 0.05) in subjects aged 35 years and above (4). It is not known if other aging processes are implicated or that ARVs or HIV cause more marked problem in the elderly, but all these factors have been implicated (2).

Majority of the patients with hearing loss had SNHL and this transcends across all the age groups. The cause of this SNHL is thought to be damage to mitochondrial DNA which could be due to toxicity of ARVs, viral toxicity or even mutations especially in the elderly. All these factors could synergise (3, 6, 8, 9).

The frequencies most affected were the higher levels of 4KHZ and 8KHZ. This is similar to reports by Chandrasekhar *et al* (1) and Rey *et al* (6), it is not clear why this is so, however, it is thought to be due to changes in cochlear mechanisms.

There was no significant correlation between hearing loss and the ARV regimes, P > 0.05 (0.42). This could be due to the fact that one or more drugs appeared in various combinations, but in a combination where the only difference was efavirence and nevirapine, no difference in hearing level was found. All patients were on combination therapy (5) hence it was difficult to know which drugs could be implicated as the worst in causing hearing loss.

In conclusion, anti - retroviral therapy does not cause hearing loss in HIV positive patients. In the initial six months, the hearing loss worsens and this could not be explained even though it is postulated that this could be attributed to the ARVs ototoxicity, the viral disease process or due to continued middle ear infections until there is improved immunity due to the ARVs usage for more than six months when gradually the hearing function improves. Patients on ARVs should be monitored closely audiologically since some ARVs have been found to be associated with hearing loss.

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