Original Article

Treatment of Multi-Drug Resistant Tuberculosis and the Associated Hearing Loss in Jos-North Central Nigeria

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ABSTRACT

Tuberculosis (TB), Human Immunodeficiency Virus (HIV) infection and malaria are ailments with global attention. Tuberculosis is very rampant in sub-Saharan Africa. Compounding factors have presented various challenges to the treatment of this disease. This article aimed to determine the extent of hearing disorder following treatment of resistant tuberculosis and provide information to help institute preventive and rehabilitation measures during the treatment. This retrospective study was carried out in APIN clinic, set up to care for HIV and related disease management. This 36-month study reviewed the pure tone audiogram of patients treated in this hospital. Data extracted included the biodata, audiometric pattern, type of hearing loss and was analyzed using tables and simple descriptive terms on SPSS version 17. Of 108 adults consisting of 76 males and 32 females, the age ranged from 17 to 73 years. The age group 31 – 40 years (37.61%) was mostly affected. The incidence of MDRTB was lowest among the professionals in 3 (2.75%). The Marital status comprised mainly the married in 57(52.8%). Sixty-two (57.4%) were HIV negative and 35 (32.4%) MDRTB patients newly diagnosed. The therapeutic agents included either kanamycin or Capreomycin as part of the initial regimen. Otolologic complaints were bilateral in 23.4% and 62.0% unilateral hearing loss respectively. Fifty nine (54.6%) had varying degrees of hearing loss. Sensorineural hearing loss in 49.54% was in majority. Forty-two patients (38.9%) benefited from hearing aids while 35.6% did not. Forty-five (41.7%) did not get hearing aids. Hearing loss from treating Multidrug Resistant Tuberculosis is a common complication and a real challenge to quality of life in our environment. The provisions for the rehabilitation in this study seems inadequate and where provided, have limited capacity to cater for profound hearing loss. Therefore there is need for interdepartmental collaboration to provide standard quality care for these patients.

Keywords: Hearing loss, Hearing aids, Multi-drug resistant, Tuberculosis, Treatment.

INTRODUCTION

Tuberculosis, human immunodeficiency virus infection and malaria are among the most common ailments with global attention.1,2 Tuberculosis is very rampant in developing world especially the sub-Saharan Africa with a huge burden as a result of poor socioeconomic, political and other factors.3 An estimation of 8.7 million new cases (13% co-infected with HIV) and 1.4 million deaths due to TB (430,000 in HIV-infected individuals) were reported in 2011. In sub-Saharan Africa, HIV is pandemic; most countries reported above 30% of patients with active TB are co-infected with HIV. Nigeria is ranked highest with TB...
burden in Africa and one of the highest in the world (311 per 100,000). As much as 210,000 new cases of all forms of TB occurred in Nigeria in 2010, with Lagos, Kano, and Oyo States having the highest TB prevalence rate. Benue has a high TB burden attributable to a high HIV prevalence. More than 2 billion people (about a third of the world's population) are estimated to be infected with Mycobacterium tuberculosis with new infections occurring in about 1% of the population each year. The WHO global TB report of 2018 reveals the incidence of MDR/RR-TB among new cases and retreatment cases of TB to be 4.5% and 2.5% respectively (using 2017 data). Compounding factors like the use of ototoxic medications for treating ear infections, malaria, cancer, human immunodeficiency virus (HIV) infection and subsequent Acquired Immunodeficiency syndrome as well as drug-resistant tuberculosis has brought various challenges to the treatment of this disease. The number of resistant Tuberculosis cases amidst unrecorded new cases is rising. This disease most often responds to traditional antituberculosis drug which are ototoxic and have resulted in a number of cases of hearing loss. Unlike Tuberculosis, hearing loss is a silent disease in which most of the sufferers’ are resident in Sub-Saharan Africa. Hearing loss has a profound impact on interpersonal communication, psychosocial well-being, quality of life and economic independence. The World Health Organization’s estimates showed that the number of people with such impairment increased from 42 million in 1985 to about 360 million in 2011. Currently the prevalence of hearing loss, degrees of hearing loss and challenges of managing the hearing loss associated with multi-drug resistant Tuberculosis treatment is unknown in my centre. This paper therefore aims to document these challenges and the way forward.

MATERIALS AND METHODS

The City of Jos is located within the North Central geopolitical zone of Nigeria. It has a population of over five hundred and ten thousand (510,000) people. The study was carried out at the pulmonology Unit of the Department of Medicine, Jos University Teaching Hospital, Nigeria, a tertiary health facility. Apart from Jos inhabitants, this center serves patients from a catchment area of over 280 kilometer radius. Only five out of about 135 Otolaryngologists in Nigeria are practicing in Jos. There is no speech pathologist/therapist presently practicing here.

Study design

It was a retrospective study of all patients aged 17-73 years who presented within the study period (January 2005 – December 2008/36 months) with complaints of hearing loss, tinnitus, or combination of tinnitus with hearing loss following commencement of the second line antituberculosis drugs.

Setting

The study setting was the Pulmonology unit of the Department of Medicine.

Patients and methods

This was a 36-month (January 2005 – December 2008) review of the folders of all patients with diagnosis of Multi-drug Resistant Tuberculosis (MDR-TB) on treatment in APIN. The biodata such as age, gender, occupation, educational level, retroviral status, treatment, duration of treatment and complication were extracted. There view of the pure tone audiogram of all patients treated in this department was also undertaken along with the audiometric pattern, type of hearing loss and pure tone average.

Methods

The pure tone audiometry was done after Otoscopy and removal of cerumen, if any. The individual patient was correctly fitted with head phones and then instructed to raise his/her hand every time the emitted sound was heard, even if very faint. The presentation of sound started at 60 dB (decibel) hearing level (dB HL) at 1 kHz. If there was no response at this threshold, it was raised in 10-dB increments until the patient responded to the sound. When the patient responded to a sound, the hearing threshold was then obtained, decreasing thresholds by 10-dB steps and increasing by 5-dB steps, until the threshold was established and confirmed on three consecutive occasions. These thresholds were established in the same manner at 2 kHz and 4 kHz, and then back to 1 kHz until they were within 5 dB of the original measurement at 1 kHz. If not, the entire
procedure was repeated. The equipment used was FA-10 audiometer (Fornix-USA) in a sound proof room.

**Statistical Analysis**

The data was analyzed using SPSS version 17 in simple descriptive terms and tables.

**RESULTS**

A total of one hundred and nine (109) Adult cases were seen out of which 108 cases completed the study with 1 deceased patient over a three-year period (January 2005 – December 2008/36 months). There were 76 males and 32 females with a male to female ratio of 2.4:1. The patients’ ages ranged from 17 to 73 years as shown in Table 1. The mean age was 35.5 years. The rest are as shown below: Table 1. Showing the Age group, Occupational Status and Marital Status

Forty two (42.6%) and 62 (57.4%) were HIV positive and Negative respectively.

There were 73 MDR-TB (67.6%) patients who were previously treated TB cases and 35 (32.4%) MDRTB patients who were newly diagnosed cases.

The overall prevalence rate of disabling hearing loss observed in the age group 17-73 years was 10.9%.

Table 1: Patients’ demographic data

<table>
<thead>
<tr>
<th>Age Group</th>
<th>No. of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>31-40</td>
<td>41.0</td>
<td>37.61</td>
</tr>
<tr>
<td>21-30</td>
<td>38.0</td>
<td>34.86</td>
</tr>
<tr>
<td>41-50</td>
<td>14.0</td>
<td>12.84</td>
</tr>
<tr>
<td>51-60</td>
<td>10.0</td>
<td>9.17</td>
</tr>
<tr>
<td>11-20</td>
<td>3.0</td>
<td>2.75</td>
</tr>
<tr>
<td>61-70</td>
<td>2.0</td>
<td>1.83</td>
</tr>
<tr>
<td>71-80</td>
<td>1.0</td>
<td>0.92</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>108.0</strong></td>
<td><strong>100.00</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Occupation</th>
<th>No. of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professional</td>
<td>3.0</td>
<td>2.78</td>
</tr>
<tr>
<td>Skilled</td>
<td>14.0</td>
<td>12.96</td>
</tr>
<tr>
<td>Semiskilled</td>
<td>38.0</td>
<td>35.19</td>
</tr>
<tr>
<td>Unskilled</td>
<td>6.0</td>
<td>5.56</td>
</tr>
<tr>
<td>Farming</td>
<td>17.0</td>
<td>15.74</td>
</tr>
<tr>
<td>None</td>
<td>31.0</td>
<td>28.70</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>108.0</strong></td>
<td><strong>100.00</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Marital Status</th>
<th>No. of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Married</td>
<td>57.0</td>
<td>52.78</td>
</tr>
<tr>
<td>Single</td>
<td>42.0</td>
<td>38.89</td>
</tr>
<tr>
<td>Divorced</td>
<td>9.0</td>
<td>8.33</td>
</tr>
<tr>
<td>Widow</td>
<td>0.0</td>
<td>0.00</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>108.0</strong></td>
<td><strong>100.00</strong></td>
</tr>
</tbody>
</table>

Disabling hearing losses constituted 25 (23.12%) made up of 13.0 bilateral (52.03%) and 9.0 (36.0%) for right and 3 (12.0%) left ears [a total of 38 ears] respectively. Sensorineural hearing loss was noted in 54 (49.54%) cases while conductive and mixed hearing loss constituted 20 (18.35%) and 35 (32.11%) respectively. Forty-two (38.9%) were provided with behind the ear hearing aids with benefit, 21 (35.6%) did not benefit from hearing aids. 45 (41.7%) did not have hearing aids.

**DISCUSSION**

The principal findings in this study include predominant male gender in the fourth decade of life with the highest incidence being among semiskilled and the married as well as Kanamycin being the main causative agent causing deafness. The main Otologic symptom and types of hearing loss were unilateral hearing loss and bilateral profound sensorineural hearing loss and inadequate provisions for rehabilitation of the hearing loss.

There was male gender preponderance of 2.4:1 in this study. The ages ranged from 17 to 73 years with a mean of 35.5 years. Our findings in a teaching hospital contrast sharply with that of Sogebi et al in a missionary hospital in Abeokuta, South West Nigeria where they had higher
number of 132 patients over a period of one year compared to ours with 108 patients in 3 years. However, the male preponderance and mean age in their study was almost at par with our findings. The exception was both the younger and older ages of 8 to 82 years at both extremes of ages in their study.\textsuperscript{11} The age group most commonly affected was in the fourth decade with 41 (37.61\%) followed by third decade in 38 (34.86\%) and sixth decade with 14 (12.85\%). Table.1. This concurs with the findings of Obot and colleagues in Portharcourt but disagrees with that of their third age group where they had older age group of 51-60 (21.0\%) in comparison to our younger age group in the same position.\textsuperscript{12} In terms of social class, the incidence was least among higher socioeconomic class and increases generally within the lower socioeconomic class with the exception of the unskilled class which surprisingly showed a marked reduction as shown in Table.1. The reason is/ was that lower socioeconomic class is associated with social and economic factors such as low income, lack of social support, low education and financial problems as was noted by both Sang and Mulu et al in Kenya and Ethiopia respectively.\textsuperscript{13, 14}

The Marital Status in our study revealed higher incidence among the married followed by singles and lastly the divorcees. Table.1. Our findings disagrees with that of Li and coworkers in China where the incidence was associated more with singles with features of low socioeconomic class as opined by Sang and Mulu et al as against our findings which is more in the married couple. Our finding concurs with that of Pang and colleagues in Hong Kong that marital status was associated with drug resistant tuberculosis.\textsuperscript{15, 16}

Though Drug resistant Tuberculosis is associated with Human immunodeficiency virus (HIV), our study had lower figure of HIV positivity compared to the HIV negative individuals (42.6\% vs 57.4\%) respectively. This findings concurs with that of many researchers respectively, however the lower number of HIV positive cases in this study may be due to both antiretroviral and antituberculosis drug compliance.\textsuperscript{17-21} This agrees with the stop tuberculosis strategy of directly observed therapy short-course (DOTS)–based tuberculosis programs which help the prevention of tuberculosis by reducing transmission through prompt identification, diagnosis, and successful treatment of Tuberculosis.\textsuperscript{1, 15, 16}

Also the preponderance of secondary tuberculosis against the primary cases in this study may result from noncompliance on antituberculosis because Tuberculosis programs struggle with increased caseloads, which increases the risk of acquired multidrug resistant tuberculosis. Surveillance data suggests that HIV infection and multidrug resistant tuberculosis may converge in several Countries.\textsuperscript{17-22} And without preventive treatment, 13.0\% of people living with HIV will develop TB.\textsuperscript{23-26} Progress is far slower in delivering trimethoprim-sulfamethoxazole preventative therapy, ART, IPT, and prevention interventions for HIV infection to clients of TB services.\textsuperscript{1, 4, 13, 14} Our study agrees with the Global incidence of higher TB cases than HIV where, an estimated 33 million persons are infected with human immunodeficiency virus (HIV) and 2.2 billion persons are infected with \textit{Mycobacterium tuberculosis}.\textsuperscript{19, 27-29} In contrast to our study where we had more negative cases of HIV infection, WHO\textsuperscript{19} and Getahun\textsuperscript{24} and co respectively found out that the risk for Tuberculosis is 20–37 times greater among persons infected with HIV, and in some countries in sub-Saharan Africa, up to 80\% of patients with TB have HIV infection.

At the beginning of the treatment, only 22.2\% of the patients were on Capreomycin based second line antituberculous drugs because of their baseline hearing loss, while the majority had Kanamycin based (76.9\%). Later 33.3\% changed to Capreomycin from the Kanamycin due to otoxicity while 43.5\% remained on Kanamycin and majority (55.6\%) completed their treatment on Capromycn due to safety issues Table2. Aminoglycosides are highly effective in the treatment of multi-drug resistant tuberculosis and gram negative infection. The ototoxic and nephrotoxic effects of aminoglycosides are well known and have limited their use although developing countries still use it widely because of their broad antimicrobial spectrum and low cost.\textsuperscript{30} Multi drug resistant tuberculosis patients are treated for at least 18-24 months with these second line antituberculosis drugs; placing them at high risk of developing aminoglycoside-induced Sensorineural hearing loss.\textsuperscript{31} Aminoglycosides affect both the vestibular and cochlear functions of the inner ear; however individual aminoglycosides exhibit variable degrees of cochleo- and vestibulotoxicity.\textsuperscript{32} Streptomycin
and gentamicin are primarily vestibulotoxic; amikacin, neomycin, kanamycin are primarily cochleotoxic. Patients are generally able to compensate for vestibular damage; however ototoxic hearing loss is permanently disabling. Hearing loss is usually gradual, and symmetrically bilateral. Our study is in tandem with several researchers such as Saunders, Duggal, Selimoglu, O'Donnell, Vaamonde and colleagues respectively. On the contrary, we did not have any noticeable nephrotoxicity with our patients probably due to compensatory mechanism by the vestibular apparatus. The overall prevalence rate of disabling hearing loss observed in the age group 17-73 years was 10.9%. This figure though slightly higher is comparable to 9.0% obtained in Sub-Saharan Africa. It is much higher than that obtained in Middle East and North Africa (3.00%) and far less than what obtains in East and Southern Asia from 22.00% to 27.00% respectively. Our study revealed higher numbers of bilateral (52.03%) and unilateral (48.00%) hearing loss and lower percentage of mild (11.90%), moderate (8.50%) and sensorineural hearing loss (49.54%) compared to that of Sogebi et al where they had bilateral (9.10%), unilateral (27.30%) and mild (67.00%), moderate (21.90%) and sensorineural (78.80%) hearing loss. Another sharp contrast is that we had over one third of our patients suffering from profound hearing loss whereas they had none in their study.

Disabling hearing losses in this study constituted a significant amount (23.12%). Mondelli and colleagues in a research in São Paulo noted the implications of disabling hearing loss acquired in adulthood, as setbacks in family, social life and in employment conditions, as well as isolation and frustration among adults with hearing loss. They stressed the importance of emotional stability in the diagnostic and rehabilitative processes in order to address the difficulties arising from social and familial factors. Odusanya and colleagues in Lagos found out lower prevalence rate. Their prevalence of disabling hearing loss was significantly higher in noise exposed subjects in 17.0% compared to non-noise exposed subjects 7.0% though the aetiological agent was noise rather than antituberculous drugs in our study. Our patients presented more with combined unilateral hearing (right or left) loss even though we had significant numbers presenting with bilateral hearing loss, tinnitus or a combination of both symptoms. These symptoms agreed with that of Palmay and Ramma and co respectively but vary slightly with their study where they had in addition to these symptoms dizziness and difficulty in speech understanding in noise. Patient self-reporting to detect early hearing or vestibular impairment is neither reliable nor sensitive. The associated drug-related hearing loss cannot be overlooked because of its implication. The best possible treatment, without iatrogenic lifelong hearing disability, is both an urgent ethical responsibility and an essential preventive response to the global burden of hearing loss. Encouragingly, new drugs to treat multidrug-resistant tuberculosis are now available. Bedaquiline and delamanid, and repurposed drugs such as linezolid and clofazimine, are now recommended and can be used as effective alternatives to injectable drugs.

The treatment of drug-resistant (DR)-tuberculosis (TB) necessitates the use of second-line injectable anti-TB drugs which are associated with hearing loss. Significant hearing loss following treatment of MDR when detected, interventions can be implemented to assist in communication. These include hearing aids, cochlear implants or other hearing impaired tools, teaching and training. In our research, forty-two (38.9%) were provided with behind the ear hearing aids with benefit, 21 (35.6%) did not benefit from hearing aids because of their profound hearing loss. Forty one point Seven percent did not have hearing aids. This finding agrees with that of Seddon et al but a slight variance with that of Fee who noted that hearing aids has limitations depending on the degree of hearing loss. For the profound hearing loss, Cochlear implant is the treatment of choice. However; none of the patients in our study with profound hearing loss had Cochlear implant surgery in disagreement with Byaruhanga and colleagues in Uganda who had Cochlear implant for their patient with MDR tuberculosis in Uganda.

Limitation

Being a single institutional study, the generalization made here may become a subject of debate.
CONCLUSION

Hearing Loss as a consequence of treating Multidrug Resistant Tuberculosis is a common complication and a real challenge to quality of life in our environment. The provisions for the rehabilitation in this study seems inadequate and where provided have limited capacity to cater for profound hearing loss. Therefore, there is need for interdepartmental collaboration to provide standard quality of care in these patients.

Conflict of Interest
None declared

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