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Hearing assessment and treatment outcome in ENT tuberculosis at a tertiary hospital in India

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Abstract

Aim An attempt has been made to observe the response of anti-Koch's treatment and the effect of anti-Koch's treatment on hearing in ENT tuberculosis patients by pure tone audiometry.

Material and methods A prospective observational study was carried out at the Government Medical College Hospital. A total of 200 cases diagnosed with tuberculosis in the head and neck regions were included in the study. Sputum/pus of patients were sent for cartridge-based nucleic acid amplification test (CBNAAT). Hearing assessment was done with PTA1 at the start of the treatment, PTA2 after the intensive phase (IP) at 2 months for newly diagnosed patients and at 3 months for previously treated patients, and PTA3 at the end of the AKT treatment given as per guidelines.

Results Among 200 ENT tuberculosis patients, 176 patients were cured with a new case regimen, and one patient was a defaulter. Among 19 patients who were previously treated cases (CAT II regimen), two patients had treatment failure, and the other 17 patients were cured. Four patients diagnosed to have multidrug-resistant tuberculosis (MDR-TB) on the initial drug susceptibility testing (DST) were given 24 months' treatment according to the recent guidelines of MDR-TB treatment regimen, and the patients were cured. In the present study of 200 patients, in the first PTA, 192 patients had normal hearing; in the second PTA, 106 patients had normal hearing; and in the third PTA, 35 patients had normal hearing. 21.7% of cases who were on aminoglycoside therapy developed significant sensorineural hearing loss in high frequency.

Conclusion Anti-Koch's treatment (AKT) has proven effective in ENT tuberculosis. All patients taking anti-Koch's treatment should be regularly monitored for hearing loss, adherence to treatment, drug-resistant variants, and local recurrences.

Keyword Aminoglycosides, Kanamycin, Multidrug-resistant tuberculosis, Ototoxicity, MDR-TB, Pure tone audiometry

Background

Tuberculosis (TB), one of the most ancient diseases of mankind, is one of the ten major causes of mortality worldwide [1]. It is an infectious disease caused by bacteria *Mycobacterium tuberculosis*. It usually affects the lungs (pulmonary TB) but can also affect other organs of the body [2]. In 2014, the World Health Assembly endorsed a new, bold plan called "The End TB Strategy." The vision was "A world free of TB-Zero TB deaths, Zero TB disease and Zero TB suffering [3]. The theme for the 2022 World Tuberculosis Day was "Invest to End TB, Save Lives." Although this theme is appropriate to refocus attention from COVID-19 to tuberculosis, it is a difficult task to achieve [4].

Tuberculosis treatment is aimed at curing and rapidly reducing disease transmission by reducing the bacillary population rapidly (interrupting transmission), preventing selection of naturally resistant strains (avoiding the emergence of drug resistance during therapy), and

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sterilizing the lesion (preventing disease relapse) [5]. Although antituberculosis regimens have an efficacy of up to 95%, treatment effectiveness (patients who are cured at the end of treatment under routine conditions) varies greatly with location, with the national average being around 70% (50–90%). One of the causes of low effectiveness is non-adherence. This can occur due to treatment default (patients stop using all medications) or incorrect medication use (patients use some of the prescribed medications) and/or irregular medication use (patients take the medications some days of the week but not every day of the week) [6, 7]. Treatment adherence is responsible both for treatment successes, and disease relapse will not occur. In order to improve adherence to tuberculosis treatment and restructure healthcare facilities, the World Health Organization (WHO) recommended the adoption of the directly observed treatment, short-course (DOTS) strategy [6].

Widespread misuse of antitubercular drugs has resulted in the emergence of drug-resistant TB including multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) globally. The highest incidence of new and MDR-TB cases in the world are seen in India. It is difficult to diagnose MDR-TB and XDR-TB as compared to regular TB [8, 9].

The treatment of drug-resistant (DR) tuberculosis (TB) necessitates the use of second-line injectable anti-TB drugs which are associated with hearing loss [10]. The injectable drugs, aminoglycosides and polypeptides, are associated with renal, hearing, and vestibular system dysfunction. The injectable anti-TB drugs selectively destroy the basal hair cells of the basilar membrane, which are required for high-frequency hearing [11]. After parenteral administration, aminoglycosides enter the inner ear fluids and the sensory hair cells. They react with heavy metal ions to form highly reactive free radicals that damage the stereocilia of sensory hair cells. Hearing loss starts with high frequency first and progresses to the speech frequencies. Damage is usually permanent. These drugs can also destroy the hair cells of vestibule [11]. Nephrotoxicity is generally reversible. These drugs can destroy the hair cells of the vestibular system and is usually permanent [12]. The ototoxic effects of aminoglycosides (AGs) lead to permanent hearing loss, which is one of the devastating consequences of multidrug-resistant tuberculosis (MDR-TB) treatment. As aminoglycoside ototoxicity is dose dependent, the impact of a surrogate measure of aminoglycoside exposure on aminoglycoside-induced hearing loss demands close attention for settings with limited therapeutic drug monitoring [13].

A large number of patients being treated for MDR-TB develop significant adverse effects that can impair their quality of life. Clinicians must consider risk benefit analysis during treatment as ototoxicity of injectable amino acid antitubercular treatment is permanent. So, PTA should be done on all MDR and XDR TB patients before starting the second-line antitubercular treatment. Early detection of hearing loss helps in preventing the progression of hearing loss. If hearing loss is found in PTA, then the patient should be shifted to another treatment schedule [12].

The aim of the present study is to assess hearing in ENT tuberculosis patients by pure tone audiometry. In addition, this study also assesses the response of AKT treatment and its effect on hearing. The rationale of the present study is to emphasize the importance of routine audiological assessment by all the patients taking AKT medications for early identification of hearing loss. Accordingly, changes can be made in their drug regimen by adjusting the dose or discontinuing the ototoxic drug if a satisfactory alternative is available.

Methods

A prospective observational study was carried out at the Government Medical College from December 2017 to July 2019. The study was approved by the institutional ethical committee. A total of 200 cases diagnosed with tuberculosis in the head and neck regions were included in the study. The following patients were excluded from the study:

- Patients with only pulmonary tuberculosis
- HIV patients with diabetes mellitus and known renal and heart diseases
- Extrapulmonary tuberculosis patients other than the ENT and head and neck regions
- Patients not willing to participate in the study

Study procedure

The method of sampling was non-random, purposive. Data was collected from the 200 patients with ENT manifestations of tuberculosis. Patients were explained about their disease process and the line of management. All the necessary information regarding the study was explained to the patients or their valid guardian. Informed written consent was taken from the patients or their guardian willing to participate in the study. Detailed history was taken from the study group to establish proper diagnosis. Thorough physical examination was done in each case.

Complete hemogram, erythrocyte sedimentation rate, chest X-ray, bacteriological studies, histopathological-cytological examination, and audiological assessment were done for all patients in the study. Samples (sputum/pus) of patients with symptoms of cough with expectoration were sent for *Mycobacterium* detection via

Ziehl–Neelsen staining and CBNAAT technique. Ultrasound of local area was done for patients presenting with swelling over the head and neck region. Fine needle aspiration cytology (FNAC) or biopsy from the node (with prior informed consent) was taken for evaluation.

All patients in the study were screened for their hearing assessment by means of pure tone audiometry, done by a qualified and licensed audiologist at the institute. Patients were followed up on 1st and 6th month for treatment and audiological assessment.

Hearing assessment analysis in patients taking AKT

Hearing assessment of all patients was done by a screening pure tone audiogram (PTA), thrice for the patients as follows:

PTA1—done at the start of the treatment.
PTA2—done after the intensive phase (IP) at 2 months for newly diagnosed patients and at 3 months for previously treated patients.
PTA3—done at the end of the AKT treatment.

For the purpose of obtaining pure tone thresholds, a single-channel LABAT clinical audiometer with earphone (TDH39) in supra-aural cushions was used. Electroacoustic calibrations were performed annually. The used audiometer was calibrated as per ANSI S3.6–2004 (American National Standards Institute, S3.6 2004) standard specifications.

The pure tone thresholds were obtained for frequencies ranging from 250 to 8000 Hz at octave intervals. Pure tone average 1 (PTA1) is calculated by taking average of frequencies 500 Hz, 1000 Hz, and 2000 Hz. In this study, we considered pure tone average 2 (PTA2) to check for high frequency loss. PTA2 was calculated by taking average of frequencies 1000 Hz, 2000 Hz, and 4000 Hz. For calculating average, 8000 Hz was not included as at 8000 Hz bone conduction cannot be done and only the degree and not the type of hearing loss can be identified.

Audiometric assessment was conducted in a soundproof room delivering pure tone stimuli to one ear at a time in the above said frequencies at various selected intensities. The reference intensity level was designated "X" dB at each frequency, which is the mean value of minimal audible threshold of pure tones in healthy individuals. Hearing threshold is taken as the lowest pure tone that was audible to the subject.

For testing air conduction, headphones (TDH39) were used, and for testing bone conduction hearing, a bone vibrator radio ear B71 was placed over the mastoid. The signals presented to the subject by an audiometer were characterized by its frequency, sound pressure level, and wave form.

The duration of various selected tones presented to patients varied between 1 and 3 s, and a minimum gap of 1 to 3 s was given between successive presentations. The patients were instructed to give signal on hearing the least sound of any sort till it ceases.

Pure tone audiometry: air conduction threshold

In this test, the threshold of hearing was measured for range of pure tones which were presented as per the modified Hughson–Westlake method, through earphones. The test was started with a 1000-Hz sound and was done on the better hearing ear first. If the threshold of hearing was supposed as normal, a distinctly audible signal at an arbitrarily presumed supra-threshold level, about 40 dB, was presented. If the patient complained of hearing loss, 60 dB was presented. In steps of 10 dB, the intensity of the pure tone was decreased, till it cannot be heard by the patient. Then, an increase of 5 dB steps was done, by delivering single pulse at each step, till it was audible to the participant. The point where the participant gave a response was the threshold. The test was then repeated in the same way with other frequencies. The opposite ear was also tested similarly. To evaluate the consistency of the test, the air conduction threshold was done again at 1000 Hz.

Pure tone audiometry: bone conduction threshold

In this test, the threshold of hearing was calculated for a range of pure tones delivered by the bone vibrator which was placed in the mastoid process of the ear. The test was done according to the conventional (Hughson–Westlake) procedure. The bone vibrator was kept over the mastoid process. The test was begun with 1000 Hz sound. A continuous, distinctly understandable tone was presented to the participants. There should be no contact between the external ear and the vibrator. In the opposite nontest ear, the earphone was placed over the ear for delivering the masking sound. The test ear was presented with a test tone of 1 to 2 s duration at supra-threshold level. If the level was audible, the presented tone was reduced in steps of 10 dB until the tone was inaudible. Later, the intensity was increased in steps of 5 dB, until the patient could hear. The threshold was the least point at which the patient responded. Then, the test was repeated at other test frequencies and also in the opposite side.

The results of PTA were plotted on the pure tone audiogram, where the *X*-axis shows the frequency of sounds in hertz and the *Y*-axis shows the sound level expressed in decibels (dB). This is used to characterize hearing thresholds in each ear for clinical assessment. The hearing threshold was then graded by the WHO grading scale.

0–25 dB—normal hearing.
26–40 dB- mild hearing loss.
41–55 dB- moderate hearing loss.
56–70 dB- moderately severe hearing loss.
71–91 dB-severe hearing loss.
>91 dB—profound hearing loss.

Data from the study was described as percentages and was statistically analyzed using the SPSS software version 22. Data collection sheets were filled in by the investigator, and it was compiled in a systematic way.

All the patients were started on antitubercular drugs according to the recent Revised National Tuberculosis Control Programme (RNTCP) guidelines of extrapulmonary tuberculosis. The treatment regimen schedule for drug sensitive new tuberculosis patients was 2 months of isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE) in the intensive phase and 4 months of isoniazid, rifampicin, and ethambutol (HRE) in the continuous phase. The treatment regimen schedule for drug-sensitive previously treated tuberculosis patients was 2 months of isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin (HRZES) and 1 month of HRZE in the intensive phase and 5 months of HRE in the continuous phase. The treatment regimen schedule for multidrug-resistant tuberculosis patients was, for rifampicin-resistant cases and isoniazid-sensitive cases or unknown cases, 6 to 9 months of kanamycin, levofloxacin, ethionamide, cycloserine, pyrazinamide ethambutol, and isoniazid (Km Lfx Eto Cs Z E H) in the intensive phase and 18 months of levofloxacin, ethionamide, cycloserine, pyrazinamide, ethambutol, and isoniazid (Lfx Eto Cs E H) in the continuous phase.

The treatment regimen schedule for multidrug-resistant tuberculosis patients (MDR TB) with INH resistance is 6 to 9 months of kanamycin, levofloxacin, ethionamide, cycloserine, pyrazinamide, and ethambutol (Km Lfx Eto Cs Z E (treatment modified based on the level of INH resistance)) in the intensive phase and 18 months of levofloxacin, ethionamide, cycloserine, and ethambutol (Lfx Eto Cs E) in the continuous phase [14] (H—INH, R—rifampicin, Z—pyrazinamide, E—ethambutol, S—streptomycin, Km—kanamycin, Ofx/Lvx—ofloxacin/levofloxacin, Eto—ethionamide, Cs—cycloserine, Z—pyrazinamide).

A daily course regimen is administered as fixed drug combination (FDC) of first-line antitubercular drugs according to the weight bands [15]. Patients were followed up monthly during the initial phase (IP) and every quarterly during the continuation phase (CP) until the completion of their treatment to assess the clinical response and to monitor the adherence to treatment. After the treatment, all patients were kept on regular long-term follow-up of up to 2 years.

Results

The present hospital-based prospective study was carried out among 200 patients attending the tertiary care center in the department of ENT and respiratory medicine OPD, casualty and inpatient department, irrespective of their gender/background/socioeconomic status. The patients were diagnosed and treated according to the protocol.

The five patients who developed significant hearing loss were on aminoglycoside treatment. These five patients showed high-frequency hearing loss. At 4000 Hz, the thresholds of these five patients at the end of the treatment were as follows: 60 dB, 70 dB, 80 dB, 50 dB, and 65 dB.

All the patients developed sensorineural hearing loss after anti Koch's treatment. One patient had mixed hearing loss in audiometry, and this may be due to the upper respiratory tract infection and temporary Eustachian tube dysfunction at the time of testing. In that patient, the conductive component was minimal and the sensorineural component was more.

Five patients developed sensorineural hearing loss after anti Koch's treatment. One patient was with mixed hearing loss, and this may be due to the upper respiratory tract infection and temporary Eustachian tube dysfunction at the time of testing or disappeared granulations bridging the gap between the ossicles after starting anti Koch's treatment. In the patient with mixed hearing loss, the sensorineural component was more than the conductive component (Table 1).

The summary of the hearing thresholds in patients according to their first, second, and third PTAs is shown in Fig. 1.

Treatment and outcome

All patients diagnosed with tuberculosis, either bacteriologically or histopathologically, were started on antitubercular drugs according to the recent RNTCP guidelines and drug sensitivity testing (DST) using the CBNAAT testing.

An effective response was seen with the 177 patients who have taken the CAT I (new case) regimen for 6 months according to the latest RNTCP guidelines for extrapulmonary TB. Except for one patient who had left the treatment in between and lost to follow-up, all other 176 patients were cured. Among 19 patients who were given CAT II regimen, as they were previously treated cases of pulmonary TB, two patients had treatment failure, and the other 17 patients were cured.

Table 1 Type of hearing loss and category of AKT regimen started on patients with significant hearing loss (total 5 patients)

Sr no	Diagnosis	Type of hearing loss	Category of treatment	Hearing assessment		
				PTA1	PTA2	PTA3
1.	TB laryngitis	Sensorineural	Previously treated	W	Mod/S	M.S/S
2.	TB laryngitis	Sensorineural	Previously treated	W	Mod/S	M.S/S
3.	Cervical lymphadenitis	Mixed	MDR	W	M.S/S	S/M
4.	Cervical lymphadenitis	Sensorineural	Previously treated	W	W	Mod/S
5.	TB of oral cavity	Sensorineural	MDR	W	Mod/S	M.S/S

W hearing within normal limits, *Mod/S* moderate sensorineural, *M.S/S* moderately severe sensorineural, *S/M* severe mixed

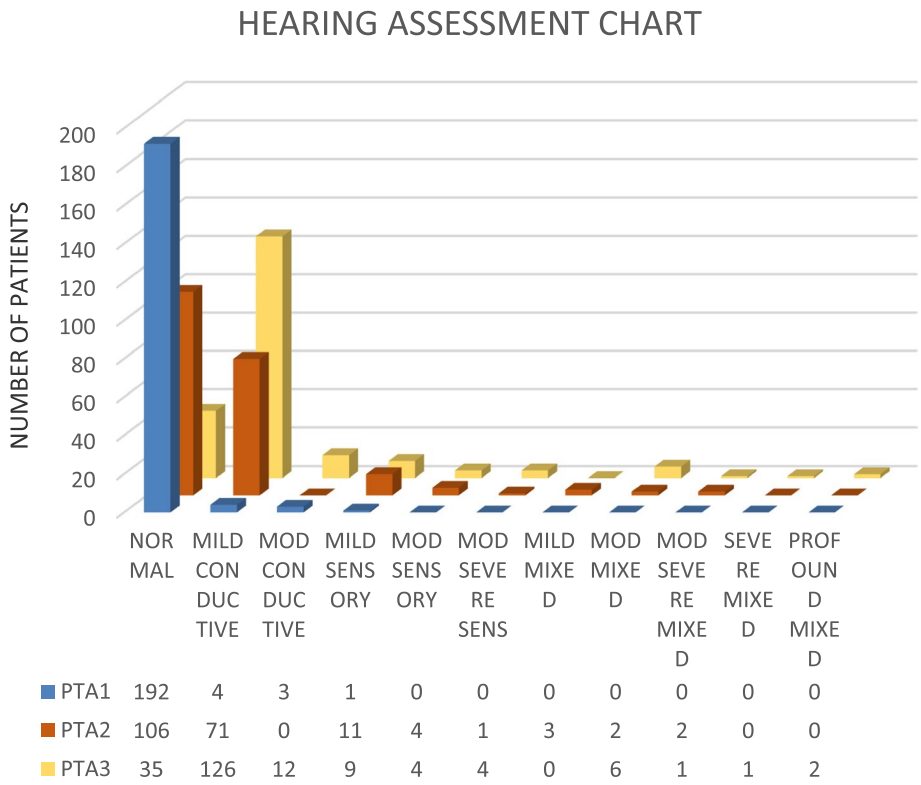

Fig. 1 Hearing assessment in each phase of treatment

Four patients diagnosed to have MDR-TB on the initial DST were given 24 months' treatment according to the recent guidelines of MDR-TB treatment regimen, and the patients were cured successfully.

Discussion

Extrapulmonary tuberculosis (EPTB) describes the various conditions caused by *Mycobacterium tuberculosis* infection of organs or tissues outside the lungs. There are many forms of EPTB, affecting every organ system in the body [16]. India has more tuberculosis (TB) cases annually than any other countries globally, with an estimated disease prevalence of 256/100,000 population [17]. Lymph node tuberculosis is seen in nearly 35% of extrapulmonary tuberculosis which constituted about 15 to 20% of all cases of tuberculosis [18].

EPTB has a significant impact on people suffering, economy, and health system. Diagnosis of EPTB is difficult, and delay in the diagnosis can cause harm. Most people with EPTB can be cured if they have diagnosis and treatment with anti-TB drugs in time [16].

Hearing assessment of patients in study

Five patients in the study had developed significant hearing loss, according to the diagnostic criteria given by the American Speech-Language-Hearing Association [19]. 21.7% of cases who were on aminoglycoside therapy developed significant hearing loss (Table 2).

Jager et al. stated that aminoglycosides are known to have some degree of toxicity to the eighth cranial nerve; both vestibular and auditory divisions may become affected. In the case of cochlear damage, hearing loss occurs as a result of degeneration of the hair cells of the cochlea, beginning at the basal coil and progressing to the apex. High-frequency hearing loss is followed by loss of lower frequencies [21].

Vaamonde P et al. reported that aminoglycosides target the sensorineural epithelium of the inner ear [22]. Outer cochlear hair cells are more vulnerable to injury than inner hair cells; the basal region is more prone than the apical region, and loss of cochlear hair cells causes secondary degeneration of the auditory nerve [23]. Injectable aminoglycosides reach the inner ear within a couple of minutes and may attain highest concentration within 30 min to 3 h following systemic administration [24]. Huy et al. identified the delayed presence of aminoglycosides in inner ear fluid after treatment [25]. In the present study, five patients developed significant high-frequency hearing loss, and they were also on injectable aminoglycoside antibiotics (Table 2).

In the early stages of ototoxicity, damage is limited to the higher frequencies and does not usually affect frequencies utilized in conversational hearing. Vestibular disturbance is found predominantly in the vestibular sensory cells from the crista ampullaris and causes ataxia and nystagmus. Neither cochlear nor ampullar cells can regenerate once they have been destroyed [26, 27].

D Rachana et al. observed in their study that patients reported reduced hearing sensitivity, tinnitus, episodic vertigo, and high-frequency SNHL irrespective of the duration of drug intake followed by administration of MDR TB drugs. In all patients, 2, 4, and 8 kHz were majorly affected. With increased exposure, this progressed to involve the lower frequencies [28]. In the present study, also, the high frequency was affected.

James A Seddon et al. stated in their study that therapeutic drug monitoring (TDM) plays a greater role in the management of patients on injectable treatment for drug-resistant TB. A large proportion of patients treated for MDR-TB are developing hearing loss, a significant adverse event that can impair their quality of life [11]. In study by Fausti SA et al., among patients showing a decrease in sensitivity corresponding with treatment, 62.5% demonstrated initial hearing loss solely in the high-frequency range, 13.5% first showed loss only in the conventional-frequency range, and 24.0% showed loss in both frequency ranges concurrently [29]. In the study by G R Voogt et al., it was found that kanamycin and streptomycin were ototoxic even at "safe" levels of drug administration, but the standard anti-TB drug combination had practically no ototoxic effect [30]. Vishal Sharma et al. in their study on 100 patients using kanamycin found ototoxicity in 18% of the subjects [31].

The first audiogram of each patient was considered as the baseline audiogram. All audiograms were obtained in a soundproof auditory test chamber with an audiometer at 250, 500, 1000, 2000, 4000, and 8000 Hz. Purushothaman et al. stated in their study that the baseline audiometric test should be done within 24 h of administering chemotherapeutic agents and within 72 h of administering aminoglycoside antibiotics. Audiological reassessment done within 24 h helps in determining patient reliability for behavioral threshold testing [32]. Most studies have found high-frequency audiometry, a more sensitive tool in the early identification of ototoxic changes than PTA. Ototoxic changes first occur at 8000 Hz and then affect the lower speech frequencies [33, 34].

According to study by Hyejeong Hong et al., the hearing of all patients should be carefully monitored while using second-line injectable aminoglycosides (AGs) through routine audiological assessments for the early detection of hearing loss. Regular audiological assessments are necessary as when a symptom of hearing loss will occur, the hair cell has already damaged [35].

Table 2 Number of patients with hearing loss

	Number of patients ($n = 200$)
Significant hearing loss*	5/200
No significant hearing loss	195/200

*Significant hearing loss, according to the ASHA (American Speech-Language-Hearing Association), can be defined as (a) 20-dB decrease at any one test frequency, (b) 10-dB decrease at any two adjacent test frequencies, or (c) loss of response at three consecutive test frequencies where responses were previously obtained [20]

Table 3 Comparison of the hearing loss in other studies

Study	Number of cases	Percentage of cases (%)
De Jager et al. [21]	11/61 cases	18
Duggal P et al. [36]	12/64 cases	18.8
Kennedy B et al. [37]	8/13 cases	61.5
Sturdy A et al. [38]	9/50	18
Present study	5/23	21.7

The World Health Organization (WHO) estimates that there are 650,000 cases globally of MDR-TB. Duggal found ototoxicity in 18.75% of the 64 subjects studied (Table 3). None of the patients had any recovery in pure tone thresholds after stopping the treatment. MDR-TB patients were treated for at least 18–24 months with the second-line TB drugs, and they tend to develop sensorineural hearing loss [36]. Similarly, in the present study, the severity of hearing loss was more at the end of the treatment than during the treatment. So, the intensity of hearing loss increases with the duration of the treatment (Table 1, Fig. 1).

Recently, the incidence of aminoglycoside antibiotics-induced deafness (AAID) has increased and is now the major cause of deafness in China [39]. This may be due to second-line injectable agents, including aminoglycosides (amikacin, kanamycin, streptomycin), and mechanistically related polypeptide drug (capreomycin) in combination with fluoroquinolones was recommended by earlier WHO guidelines for the treatment of multidrug-resistant tuberculosis [40]. Children receiving AKTs will need more attention and hearing assessments as hearing loss will result in delayed communicational development and illiteracy [41].

Treatment outcome

In the present study, an effective response was seen with the 177 patients who have taken treatment for 6 months according to the latest RNTCP guidelines for extrapulmonary TB. Except for one patient who had left the treatment in between and lost to follow-up, all other 176 patients (99.43%) were cured. Among 19 patients who were previously treated cases, 17 patients (89.47%) were cured. Two patients were not cured (10.52%), who were previously treated. Four patients diagnosed to have MDR-TB on the initial DST were given treatment for 24 months according to the recent guidelines of MDR-TB treatment regimen, and all patients (100%) were cured successfully (Tables 4 and 5). Similar results were obtained by authors in other studies.

Second-line injectable agents in conventional MDR-TB treatment regimen were associated with treatment success. Due to serious adverse events of second-line injectable agent, the WHO 2018 guideline has an option for injectable free regimens [42]. This may be the reason for failure in treatment adherence and defaulters. In the present study, 99.43% of patients who had followed the regimen strictly were cured of the disease.

A study by Soumyajit et al. done on 63 patients showed that the response to category I (DOTS) regimen was found to be effective, and 96.8% (61 cases) showed favorable response at the end of 6 months. There were only two failures (3.2%) [18].

The cornerstone of management of TB lymphadenopathy is AKT which has proven very effective in management in all studies [43]. A study by Akkara SA et al. also showed good response of patients to AKT drugs [44]. All patients with TB otitis media had complete cure with category I AKT. However, improvement in hearing was very marginal [45, 46]. Again, AKT proved to be effective in cases of TB laryngitis, but surgery may be required in cases of airway compromise due to active disease process or scarring in cured cases [47, 48]. AKT has been reported to be sufficiently effective in achieving complete cure in cases of nasal tuberculosis [49, 50].

Among 323 patients studied by Ricardiello et al., all the patients were cured after the treatment and in a 2-year follow-up; they observed that three patients were lost at follow-up, 18 patients (5.57%) had local recurrence, 17 cases had laterocervical localization, and one had a laryngeal lesion), and the remaining 302 patients (93.5%) showed no local recurrence [51].

Table 4 Treatment regimens given to the patients

Treatment category started	Number of patients
New case	177
Previously treated	19
MDR regimen	4
Total no. of patients:	200

Table 5 Treatment outcome of the patients in the study

Treatment outcome	New case (no. of cases, %)	Previously treated (no. of cases, %)	MDR-TB regimen (no. of cases, %)
No. of patients treated	177/200 (88.5%)	19/200 (9.5%)	4/200 (2%)
Cured	176 (99.43%)	17 (89.47%)	4 (100%)
Treatment failure	0	2 (10.53)	0
Defaulter	1 (0.56%)	0	0

Conclusion

All patients taking injectable aminoglycosides should therefore be carefully monitored through routine audiological assessments for the early detection of hearing loss and change in drug regimen, adding less cochleotoxic drug, to arrest the progression of hearing loss. The treatment with AKT drugs with the latest RNTCP guidelines has proven effective in the cure of extrapulmonary tuberculosis of the head and neck region. A regular follow-up of the patients should be maintained during and after the treatment for the proper monitoring of the adherence to treatment to detect any drug-resistant variants and to monitor any local recurrences.

Limitations of the study

Long-term follow-up of patients treated with AKT was not possible to see relapse and recurrence of disease.

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Informed consent to participate
Informed consent was obtained from all individual participants included in the study (or their parent or legal guardian in the case of children under 16).

Authors' contributions
Chavan RP analyzed and interpreted the patient data regarding ENT manifestations of tuberculosis. Anish Anto had collected the data and prepared the master chart. Nazir HA was a contributor in writing. Damodhar has done all audiological assessments. All authors read and approved the final manuscript.

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Availability of data and materials
All data generated or analyzed during this study are included in this published article (and its supplementary information files).

Declarations

Ethics approval and consent to participate
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional ethical committee as per ICMR guidelines and MUHS protocol by letter Pharma Dept. Dr. VMGMC, Solapur/IEC/Protocol/ENT/36/17 and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication
Informed written consent for publication of data was obtained from all individual participants included in the study. In the presence of manuscript images relating to individual participants, written informed consent for the publication was obtained from the participants (or from their parent or legal guardian in the case of children under 16).

Competing interests
The authors declare that they have no competing interests.

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