**ORIGINAL RESEARCH**

# Middle ear changes in head and neck cancer patients receiving concurrent chemoradiotherapy

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**Abstract**

**Background:**This study examined how often head and neck cancer patients who receive radiation develop middle ear infections. It is crucial to keep a close eye on patients with head and neck malignancies who are undergoing concurrent chemoradiotherapy as they are found to have a high incidence of otitis media with effusion. This emphasizes the importance of carefully monitoring and managing this condition for a better quality of life and treatment outcomes.**Design –** At a tertiary care hospital, this prospective case control study was conducted. **Methods:** Detailed otoscopy and immittance evaluation were done for all the patients with HNC who were receiving concurrent chemotherapy and then follow-up were studied at completion of CCRT and at 12 weeks. The study included 100 patients in all.**Results-** In the after 6 weeks of CCRT, CSOM, post-irradiation OME, were all caused byEBRT. 31% of cases were found to have B type of tympanogram indicating Otitis media effusion and 26 % had 'C'type indicating ET dysfunctioning. After 12 weeks of CCRT, 3% got 'B' type indicating Otitis media effusion and 5 % had 'C' type indicating ET dysfunction. These findings suggested that, when compared to the results of conventional radiotherapy, the External beam radiotherapy approach demonstrates the ability to reduce the incidences of OME and ET dysfunctioningThere is a considerablepercentage of head and neck malignancy cases who develop OME post RT, however, in most of them it resolves spontaneously.**Conclusion-**With further research, we can determine the optimal strategies to minimize the impact of otitis media with first visit follow up on these patients and help them in their fight against cancer.

**Key words:**head and neck cancer, chronic suppurative otitis media, eustachian tube dysfunction, external beam radiotherapy, chemoradiotherapy.



## Introduction

Concurrent chemoradiotherapy (CCRT) is commonly utilized for the treatment ofcancer (HNC). However, hearing loss is a common side effect. A sizable proportion of patients continue to experience this problem despite major improvements in radiation oncology [1]. On the inner ear and temporal bone, concurrent chemoradiotherapy have complicated consequences[2]. RT can result in increased conductive hearing loss, and both therapeutic approaches (CCRT) can cause sensorineural hearing loss (SNHL)[3].The underlying causes and characteristics of hearing loss related to chemotherapy and RT are the main key points discussed here.The rate of post-irradiation otitis media with effusion(OME), and ET dysfunction was the focus of this study.Cisplatin, a chemotherapeutic agent causes bilateral, dose-dependent, progressive, and irreversible signs of hearing loss[4]. The exact dosage used, the patient's age, a hereditary predisposition for platinum-based ototoxicity, any prior hearing loss, play a vital role in the wide spectrum of ototoxicity[5]. Chemoradiotherapy-related ototoxicity has been the subject of extensive research.The patients are at extremely high risk of hearing loss who receives radiotherapy in and around acoustic structures. Radiation therapy inducing hair cell death have been proposed because of processes involved in the pathways of P53, reactive oxygen species (ROS) and c-Jun N-terminal kinase (JNK)[6] Radiation therapy (RT) is crucial in the treatment of neck and head cancer, especially for addressing tumors in the

ear and temporal bone [7].Several researchers concluded that hearing can be safeguarded with EBRT giving the inner and middle ear low radiation doses. Because a significant radiation dosage is necessary for locoregional control likewise there are severe short- and long-term adverse effects due to the proximity of the treatment targets to numerous crucial tissues, like the parotid glands, spinal cord, orbits, and brainstem[8]. High radiation doses can be delivered to patients using the EBRT which is very precise preserving the nearby organs[9]. For instance, radiation damage to the middle ear can result in otitis media from transitory Eustachian tube malfunction that causes hearing impairment due to conductive damage (CHL)[10]. The size and location of the cancer has a key role to determine how much radiation penetrates the auditory system.These areas are frequently exposed to radiation beams during treatment for nasopharyngeal, oropharyngeal, parotid, and periauricular skin malignancies due to their central positions[12]. Unfortunately, this exposure can result in both acute and late toxicities in all areas of the ear [8]. Conductive hearing loss is a potential consequence for patients when the temporal bone is exposed to radiationWhen the inner ear is affected, it might show up as SNHL and conductive loss if the injury is to the middle ear or eustachian tube (ET)[12]. Through tympanic membrane thickening, middle ear changes, and ET modifications that result in serous otitis media, radiation can cause conductive hearing loss [5].A very frequent reason for conductive hearing loss is radiation-related otitis media with fluid (OME). Acute or persistent suppurative otitis media, prolonged TM perforation, the middle ear inflammation, and middle ear bone necrosis among additional middle ear complications that may lead to hearing loss in addition to OME.Following head and neck RT, the pathophysiology that underlies the development of OME appears to be multifaceted[12].Damage to the middle ear epithelium's mucosa and reduced ciliary function are possible factors. Fibrosis and mechanical obstruction may result from radiation exposure to the canal's narrowest section, the ET isthmus. The ET musculature may be dysfunctional or have advanced fibrosis, which could also hinder effective tube opening[7] . The probability of developing OME and, consequently, conductive hearing loss, appears to be correlated with radiation dosage over the middle ear and ET isthmus[18]. To prevent cisplatin induced ototoxicity, sodium thiosulfate, N-acetylcysteine, dexamethasone, a form of vitamin E, and even lactate have been studied extensively in both animal and human trials[13,14,15] .The systemic drugs are undesirable over intratympanic use because they interfere with antineoplastic effects of chemotherapeutic drug[16]. Dexamethasone may reduce cisplatin-induced hearing loss by targeting receptors in the inner ear[16]. Mineralocorticoid and glucocorticoid receptors help maintain inner ear balance and function. However, systemic administration may be limited by the blood labyrinth barrier, which can be damaged by excessive ROS production, leading to inner ear damage.Although , middle ear issues still arise, leading to ASOM, SOM, and CSOM [17,18]High radiation doses can be delivered to patients using the EBRT which is very precise preserving the nearby organs. The serious consequence or side effect of radiotherapy is a middle ear infection called acute otitis media. Acute otitis media (AOM), chronic suppurative otitis media (CSOM), and otitis media with effusion (OME) are all included in this spectrum of illnesses.This results int ear pain, persistent purulent secretions, tinnitus, hearing loss, and a decreased quality of life[17,18]. The prevalence of OME is 10% to 30% of head and neck cancer patients who had CCRT. It is observed that ET may suffer radiation damage if it is in the vicinity of radiotherapy fields, which could result in inflammatory changes and eventually fibrosis[18]. Although many individuals who had no middle ear issues before to RT experience OME as a result of the procedure. The explanation is due to the fact that fibrosis and inflammation of the soft tissue of the oral cavity, throat, and middle ear are what lead to ETdysfuntion. The ET typically malfunctions after CCRT to the middle ear and throat, leading to abnormal gas exchange in the middle ear and a higher likelihood of OME and persistent OM with or without discharge[18].OME in radiation cases of head and neck malignancies is well known among clinicians [17]. Still the literature does not provide adequate documentation. The simplest rationale is that the follow-up visits centred primarily on relapse detection rather than medication side effects.Because of higher survival rates, there is growing concern about the quality of life for cancer patients. Therefore, it is important to identify and comprehend any hearing issues that could be detrimental or impose limitations or alterations on the life of cancer patients. Better rehabilitation will be made possible by understanding these individuals' issues, constraints, and reactions when presented with communication challenges.The primary objective of this work is to thoroughly assess OME risk in patients with head and neck cancer.This evaluation came to the conclusion that there is a dearth of relevant material and that further study is required to identify individuals who are at risk of OME after chemoradiotherapy, ideally through investigating quantity connections between the ET and middle ear and OME development. Our research conducted an in-depth analysis of the risk of otitis media with effusion(OME) in patients diagnosed with head and neck cancer. Early detection and effective management of OME are crucial to minimize its impact on the well-being of patients. Our findings highlight the need for proactive measures to address this issue.

## Methods

The current investigation was carried out, at a tertiary care teaching hospital. This prospective case-control study was carried out by the ENT department and the radiation department between January 2017 and January 2021. Its purpose is to determine the occurrence of middle ear abnormalities in patients receiving intra-tympanic dexamethasone and concomitant chemoradiotherapy for head and neck malignancies in terms of maintaining their hearing status. Our focus in this inquiry was onunilateral head and neck cancers (HNCs). Out of 123 HNC patients, 100 received radiation and Cisplatin treatment. 15 declined, 8 had modified treatment, and 23 were lost to follow-up. The breakdown of HNC cases are shown in Table 1.Before each Cisplatin session, IT-dexamethasone was injected into the affected ear i.e. with ITD. The study included 32 females and 68 males. The baseline and follow-up tympanometry findings were compared between the study and control ears. People who had been diagnosed with HNCs and who intended to get EBRT as their initial course of treatment along with concomitant chemotherapy were included in the study. Individuals with a history of prior therapy for cancer as well as those with pre-existing otological issues such auditory fullness, ear discharge, hearing loss, tinnitus, or vertigo were excluded.Each participant's data was gathered independently in the presence of their attendant in a sound-treated room that was calm. All the willing patients provided written informed consent. Before beginning the treatment, a thorough case history was gathered to rule out any ear-related problems. Before doing the audiological test, a skilled otorhinolaryngologist examined both ears with otoscopy. The institutional ethical committee's approval was sought before proceeding. The study's goals were to examine the otoscopic findings and tympanometry results in patients receiving CCRT for head and neck cancers before and after treatment, and then to ascertain the occurrence of various types of tympanograms in these patients by comparing the findings at completion of CCRT treatment and then at 12 weeks. The intended patient population had EBRT for #33/66gys and 6 rounds of the chemotherapeutic drug Cisplatin for their cancer. Cisplatin was administered concurrently with chemotherapy in 500 ml of normal saline at a dose of 50 mg with a cumulative dose of 300 mg of cisplatin to every patient It was made sure that patients received enough hydration with vitamin supplements Ca and Fe.Pneumatic otoscopy revealed air-fluid levels, serous middle ear fluid, and a dull-appearing tympanic membrane with reduced mobility or tympanic retraction. OME was confirmed through tympanometry, which showed the 'B' curve. Negative middle ear pressure caused by ETwas indicated by the 'C' curve.

## Results

The current study included 100 out of 123 patients who received IT-dexamethasone in experimental ear and the other ear chosen as control. The study was completed by 68 men and 32 women. Mean age of the patients was 58.2 +/- 6.3 years (males 62.2 +/- 4.8 years and females 54.1+/-2.6 years). Patients reported improved hearing and tinnitus reduction, with some experiencing minor vertigo and pain during injection.

**Table: 1 Summarizes the illness sites of the enrolled patients. In total, 6 oral cavity, 21 nasopharynx, 35 oropharynx, 38 laryngopharynx cases were analysed in the study. All patients underwent CCRT.**

| S.No. | Types of cancers | No. of cases undergoing CCRT for experimental side ear |
|---|---|---|
| 1 | Oral cavity | 6 |
| 2 | Nasopharynx | 21 |
| 3 | Oropharynx | 35 |
| 4 | Laryngopharynx | 38 |

According to Table 2, the experimental group was presented with ‘A, As, B, C type of tympanogram, while the control group only had A type of tympanogram. The table also displays the number of ears in the experimental group.

**Table: 2- Disease site-specific percentage of ears that acquired normal pressure tympanogram /As /OME /negative middle ear pressure tympanogram**.

| | No of patients who received CCRT (n) for experimental side. | No of ears with ‘As’ curve on tympanometry | No of ears developed OME I.e , ‘B’ curve on tympanometry | ‘No of ears developed ‘C’ curve with negative middle ear pressure (> -100dapa) | No of ears developed ‘A’ curve |
|---|---|---|---|---|---|
| Oral cavity | 6 | 0 | 3/6 = 50% | 3/6 = 50% | 0 |

| | | | | | |
|---|---|---|---|---|---|
| Nasopharynx | 21 | 0 | 15/21 = 71% | 6/21 = 28% | 0 |
| Oropharynx | 35 | 5 (14%) | 9/35 =26% | 6/35 = 17% | 15(43%) |
| Laryngopharynx | 23 | 2(8.6%) | 4/23 = 17% | 9/23 = 39% | 8(35%) |
| Larynx | 15 | 3(20%) | 0/15 = 0 | 2/15 = 13% | 10(66%) |
| Total | 100 | 10 (10%) | 31(31%) | 26(26%) | 33(33%) |

When patients have finished CCRT immediately after 6 weeks and are due for their next follow-up at 12 weeks, the table 3 describes the different types of tympanograms with A, As, B, and C type of tympanograms.

**Table 3 - Tympanogram types (A, As, B, C) follow ups at completion of CCRT and at 12 weeks respectively**.

| Types | At 6 weeks post CCRT (n = 100) | At 12 weeks post CCRT (n = 100) |
|---|---|---|
| A | 33 (33%) | 86 (86%) |
| As | 10 (10%) | 6 (6%) |
| B | 31 (31%) | 3(3%) |
| C | 26 (26%) | 5 (5%) |

On tympanometry at first visit follow up, 10% of ears had As type, 31% of ears had a 'B' curve, indicating Otitis media, while 26% had a 'C' curve, indicating ET dysfunction. The type of tympanogram at second follow up was 3% got “B’ type and 5% got “C” type tympanogram and 6% got “As” type of tympanogram, showing that majority of the ears had recovered from post-RT inflammation. The type of As, B and C tympanogram got improved demonstrating a recovery in ET function and radiation induced oedema of mucosal lining of middle ear.

Table 4 summarizes the pneumatic otoscopy findings at the follow-ups. At first visit follow up , 10% of the ears had thickening of TM, 33% of the ears had normal TM, 20% had retracted TM and 37% had air-fluid levels visible through TM. At second visit follow up, 85% of ears were presented with normal and mobile TM, 5% of ears showed TM retracted, whereas 3% had air-fluid levels while majority has gone to normal and 7% had thickening of TM.

**Table 4 – Pneumatic otoscopy findings at completion of CCRT and at 12 weeks respectively**

| Pneumatic otoscopy | Experimental ear -Follow up 1 (n=100) | Follow up 2 (n=100) |
|---|---|---|
| Normal, intact & mobile TM | 33 | 85 |
| Retracted TM | 20 | 5 |
| Air fluid level | 37 | 3 |
| Thickening of TM | 10 | 7 |

Table 5 summarizes the air bone gap findings at different follow-ups time. Air bone gap considerably decreased as shown in table 5 from first to second follow up.

**Table 5 -Air bone gap at first follow up and at second follow up**

| Air bone gap (ABG) (dB) | Follow up-1 (ABG) | Follow up-2 |
|---|---|---|
| Mild conductive hearing loss | 20% | 5% |
| Moderate conductive hearing loss | 10% | 2% |

## Discussion

Our research focus on to find out meaningful solution for middle ear issues in patients who receive CCRT. For this the current study focuses on these patients at two visits. One at 6 weeks when just CCRT finished and other at 12 weeks post CCRT. In the present study, the average age of the participants was 58.2 years, and the male to female ratio was 2:1.It is consistent with findings from other research, including those by Kuo et al. that involved OME patients[19]. The latter likewise

has an age range of 46 to 55 years, with males having the highest incidence. Another study had similar findings in which incidence ofnasopharyngeal carcinoma occurs most in men due to the influenceof different male and female lifestyles[12]. For example, smoking habitsare higher in males than females. Similarly, alcohol drinking ishigher in males than females.

The second important finding is that, six weeks following CCRT, 10% of 100 ears showed As tympanic curves, 31% of them had type B curves, 26% type C curves, and 33% type A curves, which, in turn, indicated no pathology, stiffness of the TM, OME, and ET dysfunction. This is because radiotherapy caused inflammatory alterations in the eustachian tube and middle ear mucosa. The mechanical restriction that resulted from irradiating ET at its narrowest lumen caused pressure imbalances between the middle ear and the nasopharynx, which further contributed to ET dysfunction [17].Middle ear effusion, also known as OME, results from fluid building up in the middle ear if the negative middle ear pressure continues to rise. A major factor in the development of OME is the radiation dosage across the auditory structures. The risk of hearing loss is reduced if the auditory structures are preserved, as with EBRT. Ineffective ET musculature and late fibrosis may also obstruct effective tube openingcausing conductive hearing loss as a result[18].Pneumatic otoscopy, a crucial clinical procedure used by ENT, has a high sensitivity of 90% and a specificity of 80% for the diagnosis of TM disease [9]. This normal procedure alone can reveal the color, motility, any retraction or concavity, and any serous or air fluid levels. In the current study, we discovered that normal TM occurred in 33% of instances at 6 weeks and 85% of cases at 12 weeks. The amount of air fluid behind the retracted TM and its presence drops to 15% and 34%, respectively.

The present study revealed that the incidence of OME immediately following concurrent chemoradiation therapy was 31%, which dropped to 3% and incidence of ET dysfunction was 26% which dropped to 5% after 12 weeks respectively. The occurrence of OME in patients with head and neck cancer after radiation treatment can vary significantly across different studies because of variability in sites of cancer and different dosages of chemoradiotherapy[17]. The type of As, B and C tympanogram got improved demonstrating a recovery in ET function and radiation induced oedema of mucosal lining of middle ear. These results are similarto one similar study which found the incidence of Otitis media effusion was 23.2% and ET dysfunction was 19.6%[18] resolving to 1.8% and 14.3% respectively at half yearly follow up.The results of present study were in corroboration to the previous studies.OME or negative middle ear pressure also leads to reduced hearing in these patients. In the current study 30% of ears showed a conductive deafness at first follow up i.e Mild conductive hearing loss presented in 20 ears and moderate in 10 ears while 7% showed a conductive deafness at SFU on audiometry in the range of mild CHL in 5 ears and moderate in 2 ears. This present study results are in coherence to the other study which found 28.6% of ears showed a conductive deafness at FFU while 15.3% showed a conductive deafness at SFU on audiometry in the range of 10–30 dB. Even though conductive component of hearing loss was mild, if the patients previously had SNHL or develop post RT, this adds to their hearing problems[12]. The pathophysiology of the middle ear and the Eustachian tube, however, may change throughout time, most likely as a result of the resolution of ET inflammation, OME frequently end on their own, according to the available supporting studies[17,18].Thetreatmentofpost-radiationOMEremainschallengingand controversial. Several management options have beenstudied: conventional hearing aids,tympanocentesis,myringotomiesandaspiration, ventilation tube/grommet insertionwith the goal of proper aeration of middle ear and ET and hence resolving conductive hearing loss[17].Hence,, it is advised to use a conservative approach in the management of OME, relying on medications, hearing aids and regular monitoring to let the condition take its course naturally.Myringotomy is also preferrable over grommet insertion as placing grommet can cause persistent TM perforations and prolonged ear discharge, but myringotomies led to better and faster healing[17,18].

## Conclusions

The illness known as OME frequently develops after radiation treatment for head and neck malignancies. There is little information on its prevalence in other types of head and neck, despite the fact that it has been extensively researched among individuals with nasopharyngeal cancer. Otitis media and other middle ear issues are common side effects of chemotherapy and radiation therapy for those with head and neck cancer, but they usually go away on their own with time.

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