DOI: 10.7860/JCDR/2023/58318.17210

Original Article

Ear, Nose and Throat Section

Pure Tone Audiometry Findings before and after Radiotherapy in Head and Neck Cancer Patients: A Hospital-based Prospective Interventional Study

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ABSTRACT

Introduction: Radiotherapy is still the major treatment modality for Head and Neck malignancies preferred by patients as well as surgeons. Temporal bone and brain stem are mostly included in the portals. So the middle ear, inner ear and brain stem may receive a significant radiation dose causing hearing loss.

Aim: To study the effect of radiotherapy on hearing in patients with head and neck cancer.

Materials and Methods: This study was a hospital-based prospective interventional study, done in Assam Medical College and Hospital, Dibrugarh, Assam, India, from 1st July, 2020 to 30th June, 2021. A total of 33 patients with head and neck malignancies receiving radiotherapy as a mode of treatment attending Ear Nose Throat (ENT) Outpatient Department (OPD) and Department of Radiation Oncology were included. Pure Tone Audiometry was done for hearing assessment before and after radiotherapy. Microsoft excel version 2010 was used for recording the data.

Results: A total of 66 ears (33 patients) have been evaluated. Out of 33 patients, 29 patients (87.88%) had decreased hearing in one/both the ear after radiotherapy. Out of 29 patients, 19 patients (65.51%) had hearing loss less than 10 dB whereas, 10 patients (34.49%) had hearing loss >10 dB, which is considered as significant hearing loss. Among the 19 patients, 3 patients (15.78%) had hearing loss <10 dB on the same ear, i.e. on the same side of malignancy where the radiotherapy was given. Other 16 patients (48.48%) had hearing loss on both ear.

Conclusion: Effect of radiotherapy with or without chemotherapy on hearing is a well known phenomenon. This study also established the fact of hearing loss in majority of patients receiving radiotherapy.

Keywords: Chemotherapy, Conductive hearing loss, Mixed hearing loss, Sensorineural hearing loss

INTRODUCTION

Cancer is in the rise causing death all over the world. It is the second most leading cause of death globally, and is projected to rise continuously, with an estimated 12 million deaths in 2030 [1]. In India, head and neck cancers are the major cause of cancer morbidity and mortality [1]. Due to lifestyle changes and use of tobacco and smoking in the society, the prevalence of head and neck cancer is on the rise in our country. Also, the lack of awareness among people about cancer and non existence of proper cancer prevention programs have made the scenario even worse. Thus, these factors result in a late presentation and delayed diagnosis of these patients [2]. Various treatment modalities of head and neck malignancies are radiotherapy, surgery and chemotherapy, or any combination among them. Radiotherapy is still a major treatment modality preferred by patients as well as surgeons [2].

Radiotherapy comes with side-effects on normal tissues of head and neck which are relatively common and unavoidable. It depends on various factors such as the site of radiation, total dose delivered and daily fraction of radiation used. Higher the total dose or larger the daily fractions, more is the complications. Common side-effects are the mucositis, cutaneous erythema and xerostomia. Other side-effects include pain on swallowing, alteration of taste and hair loss on head, neck or face. Fatigue is also very common. The acute reactions are usually self-limited. The long term side-effects manifests many months or years after completion of radiotherapy. Organ dysfunction often manifests by cell lines with slow turn over e.g. radio-necrosis of bone. In some tissues, such as inner ear hair cells, functional progenitor cells may be lacking, resulting in greater organ system dysfunction [3]. The total recommended dose limit for use in clinical practice with fractionated and single dose radiotherapy is <60 grey (Gy) for brain and <45 grey (Gy) for cochlea [4].

Intensity-modulated radiotherapy (RT) has allowed for better dose conformation, improving dose escalation to the target and sparing of more normal tissue. For head-and-neck tumours, many normal tissue structures co-exist in this region, but our understanding of their response to RT varies by structure. Sensorineural Hearing Loss (SNHL) as a result of RT to the inner ear and cochlea is a radiation dose-limiting toxicity that needs additional investigation [5].

Since the radiotherapy used in management of head and neck tumours often includes the temporal bone and brain stem in the portals. So the middle ear, inner ear and brain stem may receive a significant radiation dose. Hearing loss is a common complication of radiation treatment, which may be conductive, sensorineural and mixed. Temporary hearing impairment can result from Eustachian tube dysfunction, radiation induced otitis media and transient vasculitis of inner ear vessels, whereas the delayed radiation induced hearing loss has been attributed to the effects of radiation on inner ear with cellular changes, inflammatory reaction and haemorrhage involving the vessel [6].

Due to various modalities of advanced treatment options available for the management of head and neck malignancies, the survival has improved significantly. Hence the hearing disability due to radiation can significantly affect the quality of life [7]. Therefore, hearing impairment is an especially morbid sequelae of head-and-neck RT. It was observed that the hearing changes started immediately after the end of the radiotherapy while some patients recover from their hearing change [8]. In the present study, the authors aimed to study the effect of radiotherapy on hearing in patients with head and neck cancer.

MATERIALS AND METHODS

The present study was a hospital-based prospective interventional study conducted in the Department of ENT and Head and Neck Surgery, Assam Medical College and Hospital, Dibrugarh, Assam, India, from 8th July, 2020 to 30th June, 2021. Ethical clearance was taken from IEC (No. AMC/EC/PG/8886).

Inclusion criteria: Patients of clinically diagnosed head and neck malignancies of either sex in age group of 20-80 years and willing for radiotherapy, histopathological examinations, regular follow-up were included in the study after taking informed consent.

Exclusion criteria: Patients having past history of hearing disability (self-reported) and chronic suppurative otitis media, severe to profound hearing loss, those already received chemotherapy or radiotherapy and those not willing to give consent for the study were excluded from the study.

Sample size comprised of the total number of patients attending ENT OPD during the study period with head and neck carcinoma and fulfilling the inclusion and exclusion criteria.

Study Procedure

All the patients included in the study were subjected to detailed history including age of the patient, gender, socio-economic status (graded according to B.G Prasad Socio-economic classification) [9], locality of the patient were recorded. Complete general, systemic and ENT examination was done. The relevant details of each patient were filled. ENT examination included otoscopy, tuning fork test, EUM (Examination Under Microscope) of both the ear was done; any previous abnormality of the ear was noted. In case of nasopharyngeal carcinoma, endoscopic examinations were done to rule out any Eustachian tube dysfunction. Clinical staging of the carcinoma using 8th edition of American Joint Committee on Cancer (AJCC) staging [10] of head and neck cancer was done and then final staging of the carcinoma was also done (after investigations). Pure Tone Audiometries (PTA) were done in all the recruited cases before and after one month of the radiation treatment. PTA: Air conduction threshold level was measured at frequencies 0.25-4 kHz and bone conduction threshold level was measured at frequencies 0.5-4 kHz [11]. Degree of hearing was classified according to the threshold and recorded [12]. Hearing loss=10 dB was considered as insignificant and >10 dB was considered as significant. All the information was recorded and assessed. Symptoms pertaining to ear, nose and throat after receiving radiotherapy were also recorded.

- Investigations performed were Haemoglobin (Hb%), Total Count (TC), Differential Leucocyte Count (DLC), Erythrocyte Sedimentation Rate (ESR), Bleeding Time (BT), Clotting Time (CT), Prothrombin Time (PT), Platelet count, Random Blood Sugar (RBS), Renal Function Test (RFT), Liver Function Test (LFT) Thyroid profile. Serological test- Integrated Counselling and Testing Centres (ICTC), Hepatitis B surface Antigen (HBsAg), Anti-Hepatitis C virus (HCV), Electrocardiography (ECG) and Chest X-ray (PA view). Biopsy was performed from the tumour/growth for histopathological examination. Fine needle aspiration from palpable neck nodes/swelling if present. Direct nasal endoscopy, video direct laryngoscopy were also performed.

  Pure Tone Audiometry before and after one month of completion of radiotherapy with or without chemotherapy were performed.

  Treatment protocol with radiotherapy alone or in combination with chemotherapy was decided by the Department of Radiation Oncology. The radiation therapy consisted of a total dose 50-66 Gy (patients receiving only radiotherapy) and 63-70 Gy (patients receiving chemo-radiation therapy); prescribed to the planning target volume 1.8-2 Gy/fraction in 5 consecutive days per week.

STATISTICAL ANALYSIS

Data were presented in tabular form mentioning the frequency of hearing loss along with percentage. Software Microsoft excel 2010 version was used for recording of all the findings.

RESULTS

Total 33 patients with head and neck cancers receiving radiotherapy with/without chemotherapy were included as sample in the study. Most of the patients belonged to 51-60 years age group (39.39%) receiving radiotherapy for head and neck cancer followed by 61-70 years age group (30.3%) [Table/Fig-1].

Demographic details of subjects	Frequency (n)	Percentage (%)
Age group (in years)		
21-30	1	3.03
31-40	5	15.15
41-50	3	9.09
51-60	13	39.39
61-70	10	30.3
71-80	1	3.03
Gender		
Male	26	78.79
Female	7	21.21
Locality		
Urban	21	63.64
Rural	12	36.36
Socio-economic class [9]		
Upper class	0	0
Upper middle class	2	6.06
Middle class	8	24.24
Lower middle class	4	12.12
Upper lower class	7	21.21
Lower class	12	36.36

[Table/Fig-1]: Demographic details of all subjects: Age, gender, locality and socio-economic class [9] of all study participants.
N=33 patients; Male: Female ratio- 3.7:1

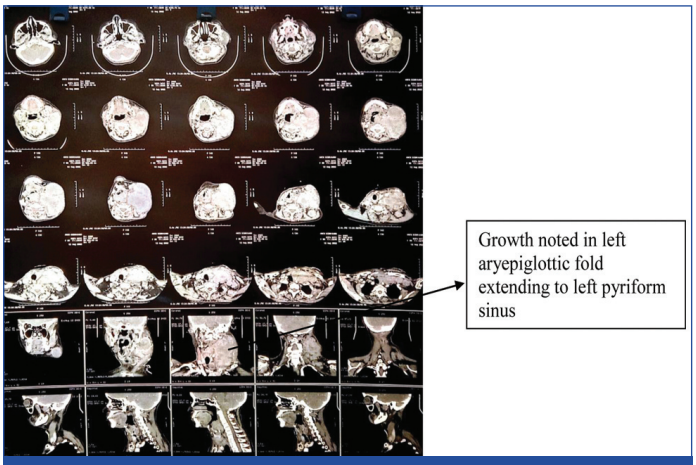
A total of 26 patients were males (78.79%) and 7 were females (21.21%) [Table/Fig-1]. In the present study, 21 cases i.e 63.64% belonged to rural areas while 12 cases i.e 33.36% were from urban areas. This study showed that majority of the patients chosen for the study belonged to lower socio-economic status [Table/Fig-1]. A total of 11 patients (33.33%) had oropharyngeal carcinoma and another 11 patients (33.33%) had laryngeal carcinoma [Table/Fig-2]. [Table/Fig-3] shows CT neck of a patient with left Aryepiglottic fold and Pyriform sinus squamous cell carcinoma.

Site of head and neck carcinoma		Frequency (n)	Percentage (%)
Oral cavity	Carcinoma tongue	4	12.12
	Carcinoma tonsil	2	6.06
	Carcinoma palate	1	3.03
	Carcinoma floor of mouth	1	3.03
Pharynx	Carcinoma oropharynx	11	33.33
	Carcinoma hypopharynx	1	3.03
Larynx	Carcinoma larynx	11	33.33
Nose/PNS	Carcinoma maxillary sinus	1	3.03
	Nasopharyngeal carcinoma	1	3.03
Total		33	100

[Table/Fig-2]: Site-wise distribution of head and neck carcinoma.
PNS: Paranasal sinus

Out of 33 patients, 25 of them received only radiotherapy, whereas 8 patients received both radiotherapy and chemotherapy [Table/Fig-4]. Out of 33 patients, 17 patients were found to be having

SNHL, 1 patient was having CHL, 7 patients were having mixed type of hearing loss. A total of 8 patients had no effect in hearing in right ear [Table/Fig-5].



[Table/Fig-3]: Computed Tomography (CT) neck of a patient with left aryepiglottic fold and pyriform sinus squamous cell carcinoma.

Gender-wise treatment distribution	Radiotherapy+chemotherapy	Radiotherapy only	Total
Male	7	19	26
Female	1	6	7
Total	8	25	33

[Table/Fig-4]: Treatment-wise distribution of the patients.

Treatment-wise distribution	Effect on hearing in right ear after radiotherapy±chemotherapy				Total
	SNHL	CHL	Mixed HL	No effect	
Radiotherapy+Chemotherapy	5	0	2	1	8
Radiotherapy only	12	1	5	7	25
Total	17	1	7	8	33

[Table/Fig-5]: Type of hearing loss after radiotherapy/chemotherapy on right ear.
*SNHL: Sensorineural hearing loss; *CHL: Conductive hearing loss; *HL: Hearing loss

Out of 33 patients, 18 patients were found to be having SNHL, 6 patients were having mixed type of hearing loss and 9 patients had no effect in hearing in left ear [Table/Fig-6].

[Table/Fig-7] shows the hearing status before and after Radiotherapy/ Chemotherapy on both ears.

Treatment-wise distribution	Effect on hearing in left ear after radiotherapy±chemotherapy				Total
	SNHL	CHL	Mixed HL	No effect	
Radiotherapy+Chemotherapy	4	0	3	1	8
Radiotherapy only	14	0	3	8	25
Total	18	0	6	9	33

[Table/Fig-6]: Type of hearing loss after radiotherapy/chemotherapy on left ear.

Hearing status		Degree of hearing preradiation		Degree of hearing postradiation	
		Right	Left	Right	Left
Normal 0-25 dB		12	16	8	9
Mild 26-40 dB	CHL	1	1	1	0
	SNHL	4	4	5	6
	Mixed	6	2	6	5
Moderate 41-55 dB	CHL	2	2	0	0
	SNHL	2	3	8	9
	Mixed	2	1	1	0
Moderately severe 56-70 dB	CHL	2	0	0	0
	SNHL	0	1	3	1
	Mixed	2	1	0	1
Severe 71-90 dB	CHL	0	0	0	0
	SNHL	0	2	1	2
	Mixed	0	0	0	0
Total		33	33	33	33

[Table/Fig-7]: Hearing status before and after radiotherapy/chemotherapy on both ears.

[Table/Fig-8] shows the hearing loss in patients pre and post radiotherapy. [Table/Fig-9] shows the distribution of hearing loss in accordance with age.

[Table/Fig-10] shows the distribution of radiation dose dependent hearing loss after radiotherapy. Distribution of patients according to audiometric changes can be seen in [Table/Fig-11].

Radiation status	Normal*	Decreased hearing	Total
Pre radiation	16	17	33
Post radiation	8	25	33

[Table/Fig-8]: Distribution of patients with hearing loss before and after radiotherapy with or without chemotherapy.
*Better ear is considered

Age group (years)	≤10 dB HL	>10 dB HL	Total n (%)*
21-30	0	1	1 (100)
31-40	1	1	2 (40)
41-50	2	0	2 (66.67)
51-60	7	5	12 (92.3%)
61-70	4	3	7 (70)
71-80	1	0	1 (100)
Total	15	10	25

[Table/Fig-9]: Distribution of hearing loss according to age.
*percentage calculated out of total patient present in that age group

Anatomical location (Carcinoma)	Number of patients	Fractioned dose (GY)	Total dose (GY)	Number of patients hearing loss seen
Oral cavity (tongue, tonsil, palate, floor of mouth)	8	1.8	70.2	5 (62.5%)
Pharynx (oropharynx, hypopharynx)	12	2	72	7 (58.33%)
Larynx	11	2	72	6 (54.54%)
Nose/PNS (maxillary sinus, nasopharyngeal carcinoma)	2	2	60	1 (50%)
Total	33			19

[Table/Fig-10]: Distribution of radiation dose dependent hearing loss after radiotherapy.

Change in severity of hearing loss	Number (%)
</=10 dB (insignificant) • Same ear (ipsilateral to side of malignancy)	3 (9.1)
• Both ears	16 (48.48)
>10 dB (significant)* • Same ears	8 (24.24)
• Both ears	2 (6.06)

[Table/Fig-11]: Distribution of patients according to audiometric changes.
*7 patients (21.21%) of oropharyngeal carcinoma had significant hearing loss (>10 dB) followed by 2 patients (6.06%) of laryngeal carcinoma and 1 (3.03%) patient of nasopharyngeal carcinoma had hearing loss more than 10 dB after one month of radiotherapy

In the present study, out of 33 cases, majority of the patients i.e. 9 patients (27.27%) presented with alterations in hearing following radiotherapy. 2 patients (6.06%) presented with ear fullness and 1 patient (3.03%) each presented with tinnitus, vertigo and nausea and vomiting [Table/Fig-12]. Other nose and throat symptoms after radiotherapy can be seen in [Table/Fig-13]. [Table/Fig-14] gives a summary of site specific distribution of hearing loss.

Complaints	Number	Percentage
Alterations in hearing	9	27.27
Tinnitus	1	3.03
Nausea and vomiting	1	3.03
Ear fullness	2	6.06
Vertigo	1	3.03
Total	14	100

[Table/Fig-12]: Distribution of patients according to symptoms (pertaining to ear).

Clinical feature	Number	Percentage
Dysphagia	2	6.06
Dryness of mouth	4	12.12
Mucositis	3	9.09
Difficulty in speech	1	3.03
Coughing	1	3.03
Localised pain	3	9.09
Others	2	6.06
Total	16	100

[Table/Fig-13]: Distribution of patients with nose and throat symptoms after radiotherapy.

Site of malignancy	Number of cases	Severity of hearing loss (>10 db HI)
Nasopharynx, PNS and nose	2	1
Oral cavity and oropharynx	19	7
Hypopharynx	1	0
Oesophagus	0	0
Larynx	11	2
Total	33	10

[Table/Fig-14]: Site specific distribution of hearing loss.

DISCUSSION

In the present study, most of the patients belonged to 51-60 years age group (39.39%) receiving radiotherapy for head and neck cancer followed by 61-70 years age group (30.3%). Only one patient (3.03%) was in the age group of 21-30 years. The mean age of the patients included in the study was 55.09 years. The youngest patient included in the study was 25 years and the oldest patient was 75 years. Most of the previous studies including that of Kaul A et.al., found that maximum number of male patients were in the age group of 41-50 years of age, whereas maximum numbers of female patients were in the age group of 51-60 years of age [13-18].

In the present study, the authors found most of the patients belonged to 5th to 6th decade of life i.e. 39.39%. However, 30.3% of patients belonged to 6th to 7th decade of life. This shifting of the age group is seen in the study done by Llewellyn CD et al. In his study he found that during the past decades, there has been an alarming rise in the incidence of oral cancer particularly among younger men, a trend that appears to be continuing [13]. In a previous study, it was seen that many younger patients had never smoked or consumed alcohol compared to older people, or duration of exposure may be too short for malignant transformation to occur. This may be the reason, older patients are more prone for cancers [13].

The present study showed male to female ratio as 3.7:1. Males are mostly affected and continue to rise in relation to the unfavourable trends in the smoking epidemic [14].

Dobrossy L in their study found out that relative to men, head-and-neck cancer is relatively rare in women. Particularly in the developed countries, men are affected more often as women, the sex ratios might exceed 10:1. In this case it corresponds to the present study [14]. Baghat S, in their study too found males were affected more than females; 23: 7, similar to the present study [15]. In the present study, 21 cases i.e 63.64% belonged to rural areas while 12 cases i.e 33.36% were from urban areas.

Siddiqui MS et al., in their study found out more number of patients of Head and Neck Cancer belong to the urban background than rural background. The study reported that Head and Neck Cancer cases are not reaching higher centres due to lesser access of healthcare among the rural population, as well as due to prevailing regional mindset, patients often resort to locally available and sometimes cheaper alternative medical therapies thus getting deprived of a proper cancer diagnosis at a higher centre. Low socio-economic status, illiteracy, ignorance of patients often act as a barrier in getting their primary symptoms of HNC checked with proper work-up; thus also preventing their diagnosis [16].

This study showed that majority of the patients chosen for the study belonged to lower socio-economic status. According to updated B.G Prasad Socio-economic classification. Class III (middle class) includes 8 (24.24%) cases. Class II, class IV and class V had, respectively 2 (6.06%), 4 (12.12%) and 7 (21.21%) cases [9]. This leads to the inference that lower socio-economic living status is an important contributing factor for advanced head and neck carcinoma, most probably due illiteracy, less medical facility, and use of firewoods during cooking.

Joshi P et al., in their study on Head and Neck Cancers in Developing Countries like India on the distribution of head and neck cancers according to socio-economic condition. They found most of the patients, approximately 90% of patients belong to lower and lower middle socio-economic group. This corresponds to the present study [17].

Amongst total patients included in the present study, maximum patients had oropharyngeal carcinoma and laryngeal carcinoma, followed by those with carcinoma of tongue, tonsil, palate and floor of mouth etc.

Siddiqui MS et al., in their study on epidemiology and histopathological spectrum of head and neck cancers in Bihar, found out that out of 173 patients with head and neck cancer, 73 patients (42.19%) had laryngeal carcinoma followed by 59 patients (34.1%) with carcinoma of oral cavity. This may be ascribed to more smoking habits in this population, specially bidi which is a form of crude cigarette [16].

In the present study, out of 33 cases, majority of the patients i.e 9 patients (27.27%) presented with decrease in hearing following radiotherapy, followed by those with ear fullness, tinnitus, vertigo and nausea and vomiting while Kaul A et al., in their prospective study on auditory alterations following radiotherapy saw most patients came with complain of ear fullness (40%) followed by decreased hearing and tinnitus (24%) [18].

Dellaringa AHB et al., in their study on audiological findings in head and neck cancer, found out 26.3% patients had hearing loss after radiotherapy for head and neck cancers. Most of them had sensorineural hearing loss [19]. Other clinical features observed were dysphagia, dryness of mouth, mucositis, difficulty in speech and pain in the localised area of carcinoma. Similar results were observed by Muller R et al., in their prospective study in patients with laryngeal carcinoma [20].

In the present study 7 patients (21.21%) of oropharyngeal carcinoma had significant hearing loss (>10 dB) followed by 2 patients (6.06%) of laryngeal carcinoma and 1 (3.03%) patient of nasopharyngeal carcinoma had hearing loss more than 10 dB after one month of radiotherapy. Anteunis LJC et al., in their prospective study on radiation induced hearing loss found out hearing loss is seen mostly in patients with carcinoma of nasopharynx, tonsils, salivary gland tumours. This is probably due to the site of the tumour which is near to the temporal bone. Thus, temporal bone too receives radiation that leads to the damage of cochlea resulting in hearing loss [11].

The present study reported radiation induced hearing loss is most commonly seen in elderly age group. Pan CC et al., in their prospective study on hearing loss after radiotherapy observed that the hearing loss is more common in elderly patient as the older patients are more susceptible to hearing loss. The effect on hearing

loss is most noticeable at the higher frequencies, especially 4000 Hz and 8000 Hz [21].

Theunissan EAR et al., in their study observed an increased risk of developing SNHL with increasing age. They stated the baseline hearing level itself is related to age. Therefore, patients with a good baseline hearing level (i.e., younger patients) may endure relatively more hearing loss (in dB) but will finish with lower threshold (in dB HL) after treatment compared to older patients. In reverse, patients with unfavourable baseline hearing levels (ie, older patients) may not have large hearing deteriorations in terms of dB, but are characterised by a higher chance of higher threshold in dB HL after treatment [22].

In the present study, authors observed that the patients receiving higher dose of radiation had more chance of hearing loss. 13 patients out of 23 patients (56.52%) receiving 72 Gy has hearing loss more than that of the patients who received 60 Gy (50%). While Mota MM et al., in their prospective study observed that an increase in the mean radiation dose to the inner ear was associated with increased hearing loss. This effect varied across frequencies, with identical radiation doses causing more hearing loss in the higher than in the lower frequencies [23].

Out of the 66 ears studied, 17 patients had sensorineural hearing loss in the right ear and 18 patients had sensorineural hearing loss in the left ear after one month of radiotherapy. Only 1 patient showed conductive hearing loss on the right ear. Eight patients in the right ear and nine patients in the left ear showed no change in hearing after one month of completion of radiotherapy. Severe sensorineural hearing loss (71-90 dB) is seen in one patient in both the ear and one patient in the left ear, same ear to the side of malignancy.

Schultz C et al., in their prospective study on hearing loss in patients with Head and Neck Cancer treated with Radiotherapy, it is seen that hearing losses of the sensorineural type predominated. But occurrences of conductive hearing losses (<0.7%) and mixed-type hearing losses (<16.3%) were also seen in either ear and in both control and study groups. They studied on 141 patients exposed to radiotherapy, out of which 102 patients had hearing loss. Sensorineural hearing loss is seen in 72 patients (51.06%). In the group of individuals exposed to radiotherapy, mild to moderate hearing losses were observed in 57.4% of right ears and 59.6% of left ears. In the control group, hearing abilities were within normal limits in 56.7% of right ears and 55.3% of left ears, and there were mild to moderate hearing losses in 42.6% and 43.3% of right and left ears, respectively; that is, the exposed group presented with hearing losses 20% more frequently [24].

Hence it can be said that the patients exposed for radiation therapy for head and cancers are in risk factors for hearing loss. A few of them recover with time while a majority of them can have permanent hearing loss.

Limitation(s)

Number of patients in the study group could have been more but because of COVID-19 pandemic, less number of patients attended ENT OPD. As the sample size is low, further studies with bigger sample size would provide concrete results.

CONCLUSION(S)

Effect of radiotherapy with or without chemotherapy on hearing is a well known phenomenon. It was established that, hearing loss occured in one or both ears, in majority of patients receiving radiotherapy.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Jun 12, 2022
- Manual Googling: Sep 27, 2022
- iThenticate Software: Oct 06, 2022 (20%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jun 08, 2022**
Date of Peer Review: **Aug 29, 2022**
Date of Acceptance: **Oct 07, 2022**
Date of Publishing: **Jan 01, 2023**