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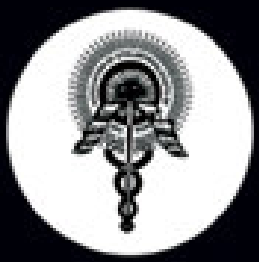

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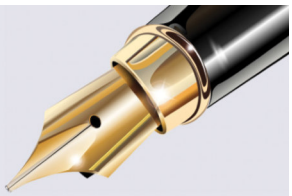
From the Desk of the Editor



Competency Based Medical Education (CBME) was defined by the International CBME Collaborators as "an outcomes-based approach to the design, implementation, assessment, and evaluation of medical curricula, using an organizing framework of competencies" (Frank, Mungroo, et al. 2010). In general, CBME is an outcome-based approach wherein the outcomes of the training have already been defined in advance and it is expected that by the time a medical student completes their training, they are competent enough to discharge their role under the five core competencies (viz., clinician, leader, communicator, lifelong learner, and professional). The advantage of any outcome-based approach is that the definition and measurement of outcomes ensure that medical learners attain the expertise required to meet the needs of patients and the health care systems. Currently many of the countries across the world is adapting CBME as the mode of training for medical graduates as well as for post graduates. In India, CBME curriculum has been implemented from the year 2019. The first batch of Students under this curriculum are just completed their internship.

The integral and essential part of any newly implemented program / curriculum is evaluation. Till date evaluation of CBME is in very rudimentary stage in our country. Within last six years, there are multiple changes / modification in curriculum as adapted by National Medical Commission. For example, Ophthalmology and Otorhinolaryngology were shifted from 3rd professional, Part I to Part II. Again these are going to revert to their previous place in Part I after 3 years. This is the high time to evaluate the effect of implementing CBME on the ultimate outcome. Few initiatives like 'Family Adaptation Program' and 'Compulsory Elective' need evaluation in terms of definite outcome and benefit to the students and also to the society. Not only NMC, but every professional body in medical fraternity should play their role in this regard. CBME curriculum in Post-Graduate stage in comparison to Under-Graduate is further less discussed, less followed and obviously less evaluated till date.

Another important aspect of implementing CBME is the need of positive approach of the faculties towards accepting new methodology of teaching learning. For this purpose different training courses (BCME, CISP) are going on under supervision of NMC regional centres. It is the responsibility of the medical faculties to make themselves well accustomed with the new methodology, providing feedback to NMC about the problems in implantation, needs for modification if any.

Dr. Sirshak Dutta
Managing Editor
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A Prospective Study of Auditory Functions in Patients Undergoing Dialysis

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Ankush Pandit,[1] Parth Makwana,[2] Vaibhav Patel[2]

ABSTRACT

Introduction

Hearing loss, as a side effect of chronic renal failure (CRF), is ignored though the incidence of sensorineural hearing loss (SNHL) among CRF patients is considerably higher than in general population. The present study was conducted in this context as an attempt (i) To find out the occurrence of SNHL viz-a-viz severity of hearing impairment in CRF patients undergoing hemodialysis. (ii) To assess HL at different frequencies in CRF patients. (iii) To study correlation between severity of HL and demographic features. (iv) To assess the factors affecting HL in CRF patients.

Materials and Methods

190 patients (age 15-70 years) who underwent hemodialysis were subjected to audiological evaluation with pure tone audiometry and impedance audiometry.

Results & Conclusion

Hearing loss has been studied in 190 CRF patients with prevalence of 61.5%. High frequency hearing loss (HL) was detected in CRF patients and only few patients had SNHL at lower frequencies. Duration of disease in CRF patients was not related to HL and there was no significant correlation between SNHL and gender, however, there was a positive correlation of SNHL with (i) stage of disease ($p = 0.016$), and (ii) age of patient ($p = 0.003$). Further, raised blood urea and serum creatinine levels couldn't predict occurrence of SNHL. Furthermore, there was no significant correlation between magnitude of HL and duration of hemodialysis and, therefore, dialysis treatment by itself doesn't alter hearing.

Conclusion

SNHL is common among CRF patients undergoing hemodialysis hence auditory screening using pure tone audiometry should be done routinely.

Keywords

Chronic Kidney Disease (CKD); Chronic Renal Failure (CRF); Hemodialysis (HD); Pure Tone Audiometry (PTA); Impedance Audiometry; Sensorineural Hearing Loss (SNHL); Blood Urea Nitrogen (BUN)

With recent advents in the field of medicine, treatment of chronic renal failure patients has changed the outcome to great extent. Morbidities have started surfacing as longevity of patients and control of renal ailments has improved. In spite of advances in treatment of CKD including hemodialysis, impairment in hearing is still a major concern in this patient. The incidence of SNHL among CRF patients is considerably higher (prevalence of 20-40%) than in general population. Various studies show that the incidence of HL in patients with CRF undergoing dialysis is within the range of 20-75% (Bazzi et al and Sahin and Varim),[1,2] 20-80% (Krishnan and Ranjit),[3] 46% (Ozturan and Lam)[4] and 40% (Bergstrom et al).[5] There are several potential factors that have been postulated in literature to contribute to the pathogenesis of HL in CKD patients. It is in this backdrop the current research project was done to ascertain the adverse impact that dialysis causes on hearing capacity of humans.

This present study was, therefore, carried out with following objectives:

(i) To find out the occurrence of SNHL viz-a-viz severity

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of hearing impairment in CRF patients undergoing hemodialysis.

(ii) To assess HL at different frequencies in CRF patients.

(iii) To study correlation between severity of HL and demographic features.

(iv) To assess the factors affecting HL in CRF patients.

Materials and Methods

This is a hospital based cross-sectional study done in a multi-specialty hospital in Vijayapura (Karnataka) during the period September 2016 - October 2018. 190 subjects with chronic renal failure (CRF) undergoing hemodialysis were assessed for audiological evaluation through otological work up which included:

(i) Otoscopy (visualization of auditory canal and tympanic membrane)

(ii) Pure tone audiometry

(iii) Impedance audiometry

(iv) Biochemical tests (Renal Function Test). Patients on aminoglycosides were not considered for the study.

Subjects with perforation of tympanic membrane, tympanosclerosis and otosclerosis were not included in the research study after otoscopic examination. Subjects (patients) were classified into:

(i) Three age groups (15-30, 31-50 and 51-70 years)

(ii) Duration of disease in three groups (<2 years, 2.1 - 4 years and >4 years), and

(iii) Hemodialysis in two groups (≤2 years and >2 years).

Informed consent was obtained from all individual participants included in the study. All procedures performed in this study were in accordance with the ethical standards of the institution and Ethical approval was taken from the Institutional Ethical Committee for the purpose of the study.

HL was comparatively studied with the above mentioned variables. Hearing impairment was classified according to pure tone average taken in WHO classification as:

(i) mild (26-40 db),

(ii) moderate (41-60 db),

(iii) severe (61-80 db),

(iv) profound (>81 db)[6]

Hearing loss was also divided, according to frequency into (i) low, (ii) mid and (iii) high frequencies.

Results

Demographic profile of patients: During the study period of two years, a total of 190 patients, subjected to dialysis, were assessed for hearing impairment. The demographic characteristics of the subjects are depicted in Table I.

Table I: Age and sex distribution of patients undergoing hemodialysis

AGE (YEARS)	TOTAL NUMBER (%)	MALE	FEMALE
15-30	40 (21.05)	28 (21.05)	12 (21.05)
31-50	80 (42.10)	56 (42.10)	24 (42.10)
51-70	70 (36.85)	49 (36.04)	21 (36.84)
Total	190 (100)	133 (100)	57 (100)

The study, on a total of 190 patients treated with hemodialysis, included 133 males (70%) and 57 females (30%). Though the age range of patients was 15-70 years, yet the entire patient population was classified into three age groups: (i) 15-30 years (40), (ii) 31-50 years (70) and (iii) 51-70 years (80).

Before undergoing hemodialysis, the diastolic BP of patients was between 90-110 mm Hg (mean 103.6). The study group was consuming diuretic (Furosemide) on everyday basis in the range of 40-200 mg (average 102.42 mg).

Prevalence of SNHL among CRF patients undergoing Hemodialysis: Hearing loss (HL) is considered as average pure tone threshold >26 db for measurement of pure tone average at frequencies of 0.5, 1.0 and 2.0 kHz.[6] Out of 190 patients undergoing dialysis 120 (61.57%)

patients had SNHL and it was absent in 70 (38.43%) patients.

Sensorineural hearing loss at different frequencies: Hearing impairment at speech frequency was registered in 17% patients (10% bilateral and 7% unilateral) while at 4000 Hz it was observed in 53.5 % individuals (47.5% bilateral and 6% unilateral). Still further, at 8000 Hz frequency SNHL was recorded in 63.1% (60.1% bilateral and 3% unilateral) patients (Table II).

Table II : SNHL in CRF patients undergoing hemodialysis at different frequencies.

FREQUENCIES (HZ)	BILATERAL (%)	UNILATERAL (%)	TOTAL (%)
500-2000	10.0	7.0	17.0
4000	47.5	6.0	53.5
8000	60.1	3.0	63.1

Table III : Sensorineural hearing loss and duration of illness ($x^2 = 2.25$, $p = 0.324$)

DURATION OF ILLNESS (YEARS)	HEARING LOSS				TOTAL	
	ABSENT		PRESENT			
	N	%	N	%	N	%
<2 years	37	44.7	44	55.0	81	100
2.1-4.0 years	22	30.1	48	70.0	70	100
>4 years	11	28.0	28	72.2	39	100
Total	70	36.0	120	64.0	190	100

N= Number of patients

As far as degree of SNHL among different frequencies is concerned, at 4000 Hz frequency mild degree of HL was recorded in 46% against the moderate HL in 6.5% subjects while moderately severe in 10 % subjects. SNHL was furter recorded at high frequency of 8000 Hz in 63.1% patients, among which 50% patients had mild degree of SNHL while 12.6 % patients were found to have moderate SNHL, as against 0.5 % patients having moderately severe SNHL. Thus, HL at 8000Hz was noticeable in 114 patients bilaterally (228 ears) and 6 patients (6 ears) unilaterally. To sum up, HL was registered in 120 patients (234 ears out of 380 ears) making an overall SNHL 61.57%. The inference from these results depicts that maximum number of patients undergoing hemodialysis had sensorineural hearing loss (SNHL) at high frequencies and only few patients had SNHL at lower frequencies i.e., 8000 Hz > 4000 Hz> 2000 Hz >1000 Hz >500 Hz.

Thus, as per the frequencies hearing loss is further classified into:

(i) Low frequency hearing loss (250-500Hz)

(ii) Mid frequency hearing loss (1000-2000 Hz)

(iii) High frequency hearing loss (4000-8000 Hz)

SNHL and duration of illness: On the basis of duration of disease, SNHL was present in 44 (55.3%) and absent in 37 (44.7%) patients who had disease for <2 years of duration and were subjected to hemodialysis. Between 2-4 years duration 48 (70%) patients had SNHL and 22 (30.1%) were normal. More than 4 years duration 28(72.2%) patients had SNHL and 11 (28%) were normal. These results indicate that maximum number of CRF patients undergoing dialysis had disease for more than 4 years of duration. Relation between duration of illness and SNHL is depicted in Table III. No association was found between SNHL and disease duration (p value = 0.324).

Tympanometry curve distribution among dialysis patients: A type curve is seen in 90.5% on tympanometry, A_s typecurve in 3% and A_d curve in 6.5% on right side while A type curve in 86%, A_s curve in 8% and A_d curve in 6.0% on left side (Table IV). Reflexes were not present in 66.5 %, present in 26% and elevated in 7.5% of subjects ipsilaterally and contralaterally in both ears (Table V). No statistically significant correlation was found between tympanometry findings and disease duration, blood variables and hemodialysis.

Table IV : Tympanometry curve among dialysis patients

TYMPANOMETRY	RIGHT (%)	LEFT (%)
A	90.5	86.0
A_s	3.0	8.0
A_d	6.5	6.0

Table V : Acoustic reflexes among dialysis patients

EAR	REFLEXES	IPSILATERAL	CONTRALATERAL
Right	Present	26.0	26.0
	Absent	66.5	66.5
	Elevated	7.5	7.5
Left	Present	26.0	26.5
	Absent	66.5	66.5
	Elevated	7.5	7.5

Table VI : Age related to SNHL ($x^2 = 8.729$, $p = 0.003$)

DURATION OF ILLNESS (YEARS)	HEARING LOSS				TOTAL	
	ABSENT		PRESENT			
	N	%	N	%	N	%
≤ 50 years	51	42.5	69	57.5	120	100
> 50 years	19	27.14	51	72.9	70	100
Total	70	36	120	64	190	100

N = Number of patients

Factors affecting SNHL in CRF patients undergoing hemodialysis:

Though the age range of patients (15-70 years) was initially classified into three groups, yet in view of the less prevalence and severity of the disease in young populations, the patient age was classified into 2 groups, ≤50 years and >50 years for assessing SNHL. A perusal of the data shows that patient, ≤50 years consisted a total of 120 patients of which 69 (57.5%) patients had SNHL and 51 (42.5%) did not have hearing loss. Patients > 50 years of age comprised of a total of 70 patients of which 51 (72.9%) had SNHL while it was absent in 19 (27.1%) patients. Relation between age and SNHL is shown in table 6. There is statistically significant correlation between age and SNHL (p value = 0.003).

As ageing is a major risk factor for hearing impairment even in healthy adults, the trend was more predominant in 65years and above. However, our study group comprised mostly of people who were lesser than 65 years.

In total 37 CRF patients were under stage 2 disease of which 13 (35.3%) had SNHL and 24 (64.7%) did not have hearing loss. In stage 3, there were a total of 39 patients of which 23 (61%) had SNHL and 16 (39%) were devoid of any SNHL. In stages 4 and 5 there were a total of 59 and 55 patients respectively among which 55 (87.5%) in stage 4 and 29 (52.7%) in stage 5 had SNHL, while 4 (12.5%) patients in stage 4 and 26 (47.3%) in stage 5 were not diagnosed to have SNHL. Relation between sensorineural hearing loss is presented in table VII. There is statistically significant association between the stage of disease (CKD) and sensorineural hearing loss (p value =0.016).

Table VII : Hearing loss and stage of disease

STAGE OF DISEASE	HEARING LOSS				TOTAL	
	ABSENT		PRESENT			
	N	%	N	%	N	%
2	24	64.7	13	35.3	37	100
3	16	39.0	23	61.0	39	100
4	4	12.5	55	87.5	59	100
5	26	47.3	29	52.7	55	100
Total	70	36.0	120	64.0	190	100

N = Number of patients

There is a statistically no significant relation between the levels of hemodialysis (p =0.727), serum urea (p=0.480), serum creatinine (p=0.945), serum potassium (p= 0.970), serum sodium (p=0.555), serum chloride (p=0.960), serum calcium (p=0.069) and serum phosphorus (p=0.852) with SNHL. Relation between laboratory values and SNHL shown in Table VIII.

Table VIII : Blood parameters of CRF patients undergoing dialysis and their effect on SNHL

S. NO.	BLOOD PARAMETERS EFFECTS	HEARING LOSS				P VALUE
		ABSENT (N = 70)		PRESENT (N = 120)		
		MEAN	SD (I)	MEAN	SD (I)	
1	Hemoglobin (Hb)	8.90	2.346	9.06	1.850	0.727
2	Blood urea	95.50	39.510	102.30	35.920	0.480
3	Serum creatinine	7.18	3.719	7.12	3.267	0.945
4	Serum	5.18	0.930	5.17	0.857	0.970
5	Serum Sodium	133.40	6.822	134.56	7.725	0.555
6	Serum chloride	102.91	6.400	102.01	6.631	0.960
7	Serum calcium	8.456	1.150	8.92	1.104	0.069
8	Serum phosphorus	5.080	1.641	5.02	1.279	0.852

Though HL in CKD patients had a significant relation with age of the patient and stage of the disease, yet there is no significant correlation between SNHL and sex, GFR (p=0.2) and diastolic blood pressure (p=0.3).

Subjects undergoing dialysis were classified in accordance to the duration of dialysis into 2 groups: (i) ≤2 years and (ii) >2 years. Out of 190 patients subjected to dialysis, 90 (47.36%) patients had a duration of dialysis less than 2 years and 100 (52.64%) patients were treated for more than 2 years. Out of 90 patients and ≤ 2 years duration HL was found in 50 patients and 40 patients did not show any HL. In 100 patients with hemodialysis >2 years, SNHL was detected in 70 patients and 30 had normal hearing (Table IX).

Table IX : Duration of dialysis and prevalence of hearing loss

DIALYSIS DURATION	HEARING LOSS				TOTAL	
	ABSENT		PRESENT			
	N	%	N	%	N	%
≤ 2 yr	40	44.4	50	55.5	90	100
2 yr	30	30.0	70	70.0	100	100
Total	70	37.0	120	62.7	190	100

N = Number of patients

Though all 190 patients underwent hemodialysis, yet there was no significant correlation between SNHL severity and dialysis duration and therefore, treatment by itself does not alter hearing.

Discussion

Hearing loss as being sensorineural (SNHL) is reported in studies evaluating the effect of renal dysfunction on hearing capacity. In the present study out of 190 patients with chronic renal failure (CRF), the prevalence of SNHL was noted only in 61.57% patients. These results were supported by studies carried out by Ali Asgar Peyandi et al[7] who found 46% end stage renal disease (ESRD) patients had SNHL and Gaur et al[8] showing an overall prevalence of SNHL to be 73.07%. In other studies, the incidence of SNHL in CRF patients on regular hemodialysis ranges from 20-75%,[7] 20-80%,[3] 75%,[9] 46%,[7] and 40%.[5] Impairment of hearing has been reported more than vestibular dysfunction. Thus, Kusakari et al[10] found that 60% of 229 patients on hemodialysis had hearing loss, 36% had vestibular dysfunction and 26% had a combination of both. In the present study, SNHL was noted maximum at high frequencies, followed by mid and low frequencies in a decreasing order. Same pattern of SNHL was observed in a prospective study conducted by Sredharan et al[11] in 25 CRF patients, 18% had SNHL at low frequencies, 32% had SNHL at mid frequencies and the remaining of them had at high frequencies. In the present study, a higher frequency hearing loss was noted in 53.5 – 63.1% patients. Almost similar results were obtained by Ozturan and Lam,[4] and Johnson and Mathog.[12] Though past studies have revealed correlations between duration of the disease, blood parameters and hearing, yet Henrich et al[13] concluded that SNHL is common in renal failure but it does not deteriorate with continuation of treatment. In the present study, SNHL was present in 44 (55.3%) and absent in 37 (44.7%) patients who had a disease for less than 2 years duration. In patients with duration of disease between 2 and 4 years, 48 (70%) patients had SNHL and 22 (30.1%) patients were normal. In case of duration of disease more than 4 years, 28 (72.2%) patients had SNHL and 11(28%) were normal. These results indicate that maximum percentage of SNHL occurred in CRF patients who had a disease of more than 4 years duration. However, no statistically significant correlation was detected between duration of illness and SNHL in the present investigation, a fact well corroborated by the studied of Jamaldeen et al[14] and Krishnan and Ranjit.[3] Contrarily, Raad Aboud Aloubad et al[15] and Lasisi et al[16] found a positive correlation between duration of illness and CRF. As far the age of the patient is concerned there is statistically significant correlation between age and SNHL (p value = 0.003). The present investigation gains further support from the earlier studies of Raad Aboud Aloubad et al.[15] Prevalence and degree of hearing loss were higher in aged population; however, this trend was more noticeable in 65 years old and above study group while our study included patients who were mostly young. A perusal of data in table 5 revealed that there is a statistically significant correlation between stage of disease and SNHL (0.016), a fact well supported by Pandey et al[17] and Krishnan and Ranjit.[3]

Though there are divergent views regarding the role of blood parameters of CKD patients undergoing hemodialysis with SNHL, yet, in consonance with the earlier studies of Samir et al,[18] and Kusakari et al[10] and Johnson et al,[19] in the present investigation also no statistically significant correlation was found between the blood parameters like levels of hemoglobin, serum blood urea, serum creatinine, serum potassium, serum sodium, serum calcium, serum chloride and serum phosphorus with SNHL. Still contrasting views regarding blood parameters vis- a- vis have been presented by different authors (Brookes,[20] Alder et al,[21] Sahin and Varim[2] and Sreedharan et al.[11]

The exact role of heamodialysis on HL is unclear but various studies have shown that it is associated with hearing loss. According to authors like Somashekara et al[22] high frequency HL seen in CRF patients is related to duration of disease, duration of hemodialysis and internal hemostasis through levels of serum electrolytes and nitrogenous products of metabolism (uremic nephropathy). This view gains further support from the earlier studies of Sahin and Varim[2] and Bazzi et al[1] who concluded that HL was higher in CRF patients undergoing hemodialysis

for over 10 years. However, Tyler and Tyler[23] suggested that regular dialysis treatment does not seem to effect HL for at least the first five years of treatment. In a noteworthy study contrasting opinion was created by Jamaldeen et al,[13] who inferred that hemodialysis sessions were inversely proportional to hearing loss but not with duration of disease, suggesting beneficial association between increasing number of dialysis sessions and SNHL.[14] Conversely, duration of disease has no relation with HL in CKD patients on hemodialysis, a fact well supported by our studies also. However, hemodialysis may have an ameliorative effect on HL in CRF patients. The above authors further advocated the beneficial role of hemodialysis vis -a- vis. HL in CKD patients since it tends to bring down the risks of HL as it increases the stabilization and correction of metabolic changes caused by CRF. Hence, appropriate treatment of CKD has to be started at the earliest in order to stop damage to organs (like dysfunction of auditory pathway and inner ear).[24]

Conclusion

Over a period of time, CRF patients undergo changes in their metabolic variables and hemodynamic status. We can't pinpoint the definite cause responsible for hearing loss in these patients. The raised blood urea and serum creatinine levels do not predict the occurrence of the SNHL. Further, our study revealed that there was no significant correlation between hearing loss severity and hemodialysis duration and therefore, hemodialysis treatment by itself does not alter hearing. It is also inferred that though hemodialysis is not a causative factor for SNHL but there is relationship between SNHL and CRF in high frequencies. Thus, hemodialysis presumably may have an ameliorative effect on hearing loss in CKD patients.

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Main Article

Microbial Profile of Tracheal Aspirates in Pediatric Tracheostomised Patients at a Tertiary Centre

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ABSTRACT

Introduction

Tracheostomy is a surgical procedure in which an opening is created between the external environment and trachea bypassing the upper airway. The presence of microorganisms colonizing the tracheobronchial airway of tracheostomised patients can potentially increase the risk of lower respiratory infections, failure of decannulation and poor surgical outcomes. The aim of the present research work was to study the microbiological profile of the tracheal aspirates and its antibiotic sensitivity in paediatric patients who had undergone tracheostomy.

Materials and Methods

The present study was conducted at the department of Otorhinolaryngology at a paediatric tertiary care hospital between August 2023-2024. 59 paediatric tracheostomised patients aged 1 day-18 years were included in the study. Tracheal aspirate obtained during regular tube changes was tested for the presence of microorganisms and their antibiotic sensitivity.

Results

Of the 68 patients who underwent tracheostomy tube changes, 59 were included in the present study. 91.53% of the study population tested positive for microbial growth in the tracheal aspirate. Pseudomonas aeruginosa (69.49%) was the most common organism isolated. 10.17% showed methicillin resistant Staphylococcus aureus (MRSA) and were positive for airway granulations.

Conclusion

Despite the numerous benefits of tracheostomy, the presence of tracheostomy tube in the airway acts as a contributing factor for the colonization of pathogenic bacteria. Presence of biofilm forming microorganisms in the airway can increase the risk of lower respiratory infections, decreased potential for decannulation and increased risk of airway surgical failure.

Keywords

Tracheostomy; Tracheal Aspirate; Culture & Sensitivity; P. Aeruginosa; MRSA

Tracheostomy is one of the oldest surgical procedure on record dating back to 3000 BC in Egypt.[1] It is a life-saving procedure in which the trachea is exteriorized creating a surgical opening between the external environment and trachea bypassing the upper airway.[2] It is done to relieve the airway obstruction and to assist in long-term ventilation support.[3] The tracheostomy acts as an alternative means of maintaining airway in patients with prolonged endotracheal intubation.

Bacterial colonization can occur following tracheostomy. The microorganisms can colonize the tracheobronchial airway of patients with tracheostomy tubes, which increases the risk of adverse respiratory events.[4-6] Long term and persistent airway colonization

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may increase the susceptibility to symptomatic infections. Additionally, patients with persistent colonization undergo antibiotic treatment and develop purulent tracheobronchitis.[7] Paediatric patients undergoing airway reconstruction surgeries have shown a high prevalence of airway bacterial colonization (MRSA; up to 32.5%). Some authors have also reported that preoperative treatment of MRSA colonization results in decreased postoperative infections and overall increased surgical success.[8]

One of the main mechanisms of tracheostomy tube colonization by pathogenic microorganisms is biofilm formation. Biofilms are present on more than 90% of tracheostomy tubes within 7 days of insertion.[9] They are associated with an increased risk of persistent airway and wound infections. It becomes imperative to identify and initiate appropriate treatment against the isolated organisms in order to prevent tracheostomy tube related complications.

The aim of the present research work was to study the microbiological profile of the tracheal aspirates in paediatric patients who had undergone tracheostomy. In addition to this we also studied the antibiotic sensitivity of the isolated microorganisms from the tracheal aspirate of these patients.

Materials and Methods

The present study is a prospective observational cross-sectional study which was conducted at the department of Otorhinolaryngology at a paediatric tertiary care hospital between August 2023- 2024. Study was conducted with ethical approval from institutional review board.

59 paediatric tracheostomised patients aged 1 day-18 years during the study period were included in the present study. Tracheal aspirate was obtained during regular tube changes.

Tube changes done in an emergency setting or patients not consenting for the study were excluded from the study population.

Samples were collected in sterile containers and mixed with sterile saline solution and sent to the microbiology department. The obtained samples were evaluated with 10% KOH, Gram staining and bacterial culture.

All the data was collected and tabulated into the SPSS version 20.0 computer software for result analysis. All means were presented with standard deviation (SD) values. Descriptive statistics, such as percentages were used to describe the cultured microorganisms in the study subjects. Fisher's exact test was used to determine if there was a non-random association between the categorical variables. A value of $p < 0.05$ was considered statistically significant for all analyses.

Results

A total of 68 tracheostomy tube changes were done during the study period, of which 59 were considered as per the inclusion criteria. Of these 59 patients, 36 (61.02%) were males and 23 (38.98%) females (Table I). 7.02 +/- 3.4 years was the mean age in our study population. The most common indication for tracheostomy in our study population was neurological causes (52.54%) followed by airway obstruction (28.81%) (Table II).

Table I: Gender Distribution

GENDER	NUMBER	PERCENTAGE
Males	**36**	**61.02**
Females	**23**	**38.98**
Total	**59**	**100.00**

Table II: Indications for Tracheostomy

SL. NO	INDICATION	NUMBER	PERCENTAGE
I	AIRWAY DISORDERS	17	28.81
	Laryngomalacia	3	5.08
	Subglottic stenosis	3	5.08
	Tracheomalacia	4	6.78
	Vocal cord palsy	5	8.47
	Tracheal stenosis	1	1.69
	Laryngeal cleft	1	1.69
II	NEUROLOGICAL CAUSES	31	52.54
	Guillain Barre Syndrome	9	15.25
	Encephalitis	5	8.47
	Meningitis	1	1.69
	Diffuse Axonal Injury	4	6.78
	Ataxia Telangiectasia	2	3.38
	Neurogenic Stridor	2	3.38
	FIRES Syndrome	2	3.38
	Lupus Encephalitis	1	1.69
	Brain Tumour	2	3.38
	Seizure Disorder	3	5.08
III	PULMONARY CAUSES	6	10.16
	Severe Pneumonia	6	10.16
IV	CARDIAC CAUSES	1	1.69
	Post VSD Repair	1	1.69
V	SYNDROMIC CAUSES	4	6.77
	Pierre Robin Sequence	3	5.08
	Edward Syndrome	1	1.69

Patients who underwent tracheostomy tube change during the study period underwent culture and sensitivity of the tracheal aspirate. 54 (91.53%) patients in our study population showed a positive culture of the tracheal aspirate. Of these positive cultures, 25 (46.29%) showed a single organism and 29 (53.71%) patients showed multiple organisms in the tracheal aspirate.

Most of the tracheal aspirates in our study population showed gram negative organisms (93.22%). The most common organism noted was *P. aeruginosa* which was seen in 41 (69.49%) patients, followed by *Klebsiella pneumoniae* in 17 (28.81%) patients. Methicillin resistant *S. aureus* (MRSA) was seen in 6 (10.17%) patients. 5 (8.47%) patients showed no growth and had a sterile culture (Table III).

Table III: Microbiological Profile of Tracheal Aspirates

SL. NO	MICRORGANISM	NUMBER	PERCENTAGE
1.	*Pseudomonas aeruginosa*	41	(69.49)
2.	*Klebsiella pneumoniae*	17	28.81
3.	Methicillin resistant *Staphylococcus aureus*	6	10.17
4.	*Acinetobacter baumannii*	8	13.55
5.	*Proteus mirabilis*	7	11.86
6.	*Morganella morganii*	3	5.08
7.	*Escherichia coli*	4	6.78
8.	No Growth	5	8.47

P. aeruginosa showed variable resistance to gentamycin, amikacin, ceftazidime and piperacillin/tazobactam. It showed 100% sensitivity to antibiotics such as ciprofloxacin, meropenem and imipenem. *K. pneumoniae* was found to be mostly sensitive to piperacillin, meropenem and imipenem antibiotics. Patients showing MRSA as the predominant culture organism was found to be sensitive to only linezolid antibiotic (Table IV).

Table IV: Antibiotic sensitivity of isolated microorganisms

SL. NO	MICROORGANISM & ANTIBIOTIC TESTED	NUMBER OF SAMPLES	ANTIBIOTIC SENSITIVITY
1.	*P. aeruginosa*	*41 (69.49%)*	
	Gentamycin		0 %
	Amikacin		0 %
	Ceftazidime		36.58%
	Ciprofloxacin		100%
	Piperacillin/ Tazobactam		65.85%
	Meropenem		100%
	Imipenem		100%
2.	*K. pneumoniae*	*17 (28.81%)*	
	Gentamycin		0 %
	Amikacin		29.41%
	Ceftazidime		64.70%
	Ciprofloxacin		88.23%
	Piperacillin/ Tazobactam		100%
	Meropenem		100%
	Imipenem		100%

Table IV (Contd.)

Table IV (Contd.) : Antibiotic sensitivity of isolated microorganisms

SL. NO	MICROORGANISM & ANTIBIOTIC TESTED	NUMBER OF SAMPLES	ANTIBIOTIC SENSITIVITY
3.	*Methicillin Resistant S. aureus*	*6 (10.17%)*	
	Benzylpenicillin		0 %
	Erythromycin		0 %
	Sulfamethoxazole /Trimethoprim		0 %
	Vancomycin		0 %
	Clindamycin		0 %
	Linezolid		100%
4.	*A. baumannii*	*8 (13.55%)*	
	Gentamycin		0 %
	Amikacin		33.33%
	Ceftazidime		66.66%
	Ciprofloxacin		83.33%
	Piperacillin/ Tazobactam		100%
	Meropenem		100%
	Imipenem		100%
5.	*P. mirabilis*	*7 (11.86%)*	
	Gentamycin		71.42%
	Co-trimoxazole		100%
	Amikacin		85.71%
	Ceftazidime		100%
	Ciprofloxacin		100%
	Piperacillin/ Tazobactam		100%
	Meropenem		100%
	Imipenem		100%
6.		*M. morganii*	*3 (5.08%)*
	Gentamycin		100%
	Co-trimoxazole		100%
	Amikacin		100%
	Ceftazidime		50%
	Ciprofloxacin		100%
	Piperacillin/Tazobactam		100%
	Meropenem		100%
	Imipenem		100%

Table IV (Contd.)

Table IV (Contd.) : Antibiotic sensitivity of isolated microorganisms

SL. NO	MICROORGANISM & ANTIBIOTIC TESTED	NUMBER OF SAMPLES	ANTIBIOTIC SENSITIVITY
7.	*E. coli*	*4 (6.78%)*	
	Gentamycin		60%
	Co-trimoxazole		100%
	Amikacin		80%
	Ciprofloxacin		100%
	Piperacillin/Tazobactam		100%
	Meropenem		100%
	Imipenem		100%

Discussion

The present study was conducted in a paediatric tertiary care hospital to evaluate the microbiological profile of tracheal aspirates in paediatric tracheostomised patients.

Of the 68 patients who underwent tracheostomy tube change during the study period, 59 patients were considered in our study. 36 (61.02%) were males and 23 (38.98%) females and 7.02 +/- 3.4 years was the mean age noted in our study. This was in accordance to a literature review of 19 similar studies done by Barros et. al.[10] in which 84% of their study population was males and 7.5 years was the mean age recorded.

91.53% of our study population showed positive pathogenic colonization of the tracheal aspirates. This was in accordance to other studies noted in literature which showed positive bacterial colonization in tracheostomised patients [11-12]. The most common organisms noted in our study were gram negative organisms such as *P. aeruginosa* (69.49%) followed by *K. pneumoniae* (28.81%). In a study done by Saravanam et. al[13] *P. aeruginosa* was the most common organism isolated from tracheal aspirates of 100 tracheostomised patients. Similarly in another study done by Vedhapoodi et al[14], *P. aeruginosa* was the most common organism noted in tracheal aspirates on day 1 (40%) and day 8 (45%) of tracheostomy. These studies were in accordance to our present study where *P. aeruginosa* was the most common bacterial colonization in the tracheal aspirates noted.

Methicillin resistant *S. aureus* (MRSA) is a major nosocomial pathogen and its incidence has been increasing in the community and in hospitals. The presence of MRSA in tracheal aspirates have an increased tendency to cause complicated lower respiratory infections. In a study done by Ahmed et al[15] on 37 children with tracheostomy tubes, children with MRSA had increased hospitalizations and intensive care admissions compared to children with methicillin sensitive *S. aureus* (MSSA). In our study MRSA was noted in 6(10.17%) patients. All these patients had increased suprastomal and infra-tip granulations on rigid laryngotracheobronchoscopy which was statistically significant (p value <0.05). These patients were sensitive to linezolid and showed resistance to most other antibiotics. Use of routine antibiotics in these patients will not be effective in controlling infections and granulations. This was in accordance to the study by Vedhapoodi et. al[14] where the tracheal aspirate with MRSA showed resistance to all antibiotics except linezolid.

Gram negative organisms such as *Pseudomonas*, *Klebsiella*, *Proteus* species etc are common colonization in tracheostomy patients.[7] These microorganisms produce an extracellular polysaccharide matrix which binds to implants or external surfaces resulting in biofilm formation.[16] It results in increased resistance to antimicrobials causing more infections in tracheostomised children. In our study, pseudomonas was found to show variable resistance to antibiotics such as gentamycin, amikacin and ceftazidime and showed 100% sensitivity

to higher antibiotics such as meropenem, imipenem and ciprofloxacin (table IV). Their ability to form biofilms helps them evade the antimicrobial action and hence can persist in the tissue environment for much longer periods. This can predispose the tracheostomised patient to more respiratory infections with complications.

In recent years, there have been significant improvements in airway reconstruction surgeries endoscopically and through the external access. This has allowed an increasing number of children to be decannulated. Presence of postoperative infections can decrease the overall surgical success rate due to loss of graft and wound sepsis.[17] The presence of bacterial colonization and biofilm formation in tracheostomised patients may result in failure of the airway reconstruction surgeries.[18,19] The knowledge of the nature of pathogens colonizing the airways can direct in appropriate management, prevent postoperative infections, reduce surgical failures and avoid the use of antibiotics of an inadequate spectrum.

Conclusion

Despite the numerous benefits of tracheostomy, multiple studies show the potential complications associated with it. The presence of the tracheostomy tube in the airway acts as a medium for colonization of pathogenic bacteria. The presence of MRSA in the tracheal aspirates was associated with increased persistence of suprastomal and infra-tip granulations. The most predominant bacteria found in our study was gram negative bacteria such as *P. aeruginosa*, *K. pneumoniae* etc. which have a potential to form biofilms. This can lead to increased risk of lower respiratory infections, decreased potential for decannulation and increased risk of airway surgical reconstruction failure in the paediatric population.

Hence it is imperative for the treating doctors to identify the pathogenic organisms colonizing the airway and their antibiotic sensitivity in paediatric tracheostomised patients for better overall management and surgical success of these patients.

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Main Article

Ototoxicity and Its Early Diagnosis in Patients Receiving Cancer Chemotherapy – A Prospective Clinical Study

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ABSTRACT

Introduction

Antineoplastic drugs play an important role in the treatment of cancer at different levels & are the most cited ototoxic agents. The main aim of this study is early detection of ototoxicity in individuals receiving chemotherapy as an attempt to reduce the challenge in diagnosis and management of ototoxicity.

Materials and Methods

A prospective study was conducted at a tertiary care center in the Departments of Otorhinolaryngology & Oncology from October 2019 to September 2021 among 140 cancer patients. Baseline audiological evaluation was done using DPOAE and Pure Tone Audiometry at baseline ,followed by within 24 hours, at the end of third & the sixth month.

Results

81.4% study subjects received combination chemotherapy, among that 21% received a combination of a Taxane and a Platinum derivative & the rest received single drug regimen. Ototoxic effects were assessed in terms of tinnitus ,vertigo & hearing loss. There was a significant hearing loss of 15 dB from baseline in high frequencies were observed in patients receiving taxanes, platinum compounds or both.

Conclusion

The study findings has led to the conclusion that ototoxic effects were more pronounced among the study subjects who had recieved Taxanes ,Platinum compounds or both (Taxanes & Platinum). Hence it is recommended that audiological assessment at base line and at all stages of the therapy should be established as a protocol to be followed in patients receiving cancer chemotherapy.

Keywords

Ototoxicity; Pure Tone Audiometry; DPOAE

Cancer is considered to be a global burden, leading cause of death & a hurdle to extend the life expectancy. According to the estimates of the GLOBOCAN database 2020 in concurrence with the WHO there is a surge in the incidence around 19.3 million and 10 million cancer deaths world-wide. This global surge in cancer leads to the likely use of antineoplastic drugs, which assist in the prevention of proliferation, invasion and metastasis of cancer cells.[1]

The term " Chemotherapy" was first coined by a German chemist Paul Ehrlich in 1900 & defined it as use of chemicals to treat a disease. The field of cancer therapy was dominated by surgery and radiotherapy until the accidental discovery of the first chemotherapeutic agent nitrogen mustard gas during World War II. The National Cancer Act was passed in 1971 that reiterated the benefits of cancer chemotherapy.[2]

Drug ototoxicity is defined as a transient or permanent, acquired hearing disorder of auditory or vestibular function

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which is usually bilateral & progressive, induced by therapeutic agents. The most common symptoms reported till date are tinnitus , hearing loss and vertigo.[3]

The American Position statement on provision of ototoxic monitoring by audiologist states that audiological monitoring for ototoxicity is done mainly for two main reasons. First and foremost is to express the principle of early identification & also to embrace the principle of early intervention. Audiological monitoring for ototoxicity still remains to be a part of active research topic even in the recent era.[4]

Audiological methods that are potentially in value for monitoring drug toxicity includes basic audiological assessment, High Frequency Audiometry (HFA) and Otoacoustic Emissions (OAE).[4]

The current study is aimed to determine the ototoxic effects of the most commonly used chemotherapeutic drugs, to establish a standard feasible ototoxicity monitoring protocol for its early diagnosis & to efficiently manage ototoxicity following cancer chemotherapy.[4]

Materials and Methods

A prospective clinical study was conducted in the Departments of Otorhinolaryngology & in the Department of Oncology at a tertiary care center in Bangalore from October 2019 to September 2021. All the diagnosed cancer patients above the age of 18 years attending the Oncology department for cancer chemotherapy were included in the study. Individuals with prior history of ear disease, ear surgery, noise exposure or trauma, patients with severe to profound hearing loss & patients below 18 years of age were excluded from the study. All the patients enrolled in the study underwent PTA & DPOAE tested at frequencies 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 4000 Hz and 8000 Hz were assessed at baseline, within 24 hours of receiving the 1st cycle, within 24 hours of receiving the 2nd cycle, within 24 hours of receiving the 3rd cycle, 03 months from start of chemotherapy & 06 months from start of chemotherapy. During all the cycles after chemotherapy, PTA and DPOAE were done only after stabilization of the patient. Those patients who reported tinnitus & vertigo after receiving chemotherapeutic drugs during any one of the cycle after commencement of treatment were also followed up.

Pure Tone Audiometry (PTA): The Pure Tone Audiometer used for our study is Arphi Diagnostic Audiometer 2001 SN 657 model & was calibrated by the audiologist daily. The hearing loss were measured by the Ototoxicity grading scales given by the National Cancer Institute & Common Terminology Criteria For Adverse Events (CTCAE) Ototoxicity Grades for children.

The NCI CTCAE ototoxicity grades for children **(with adult guidelines in parentheses) are as follows**

Grade 1: Threshold shift or loss of 15-25 dB relative to baseline, averaged at two or more contiguous frequencies in at least one ear (same for adults);

Grade 2: Threshold shift or loss of >25-90 dB, averaged at two contiguous test frequencies in at least one ear (same for adults);

Grade 3: Hearing loss sufficient to indicate therapeutic intervention, including hearing aids (e.g., >20 dB bilateral HL in the speech frequencies; >30 dB unilateral HL; and requiring additional speech language related services) (Adults: >25-90 dB, averaged at three contiguous test frequencies in at least one ear);

Grade 4: Indication for cochlear implant and requiring additional speech language related services (Adults: profound bilateral hearing loss >90 dB HL).

Note: For children without baseline evaluation, baseline thresholds are assumed to be <5 dB HL.[4]

Distortion Product Oto Acoustic Emissions (DPOAEs) : The DPOAE model used in our institution for all patients were Neurosoft 5 vorouin str Ivanovo model SN 05150W.The results were interpreted either as pass or refer.

Data Management & Statistical Analysis:

Data collected from the patients were analyzed using SPSS software version 16.0. Quantitative variables were summarized as mean, standard deviation & median. Qualitative data were expressed in terms of frequency and proportion. For the purpose of bivariate analysis, the whole data set had been reclassified into five groups based

on the chemotherapeutic agent received. Of which **1**-Taxane, **2**-Platinum derivatives, **3**-Taxane & Platinum derivative, **4**-Multiple drug regimen & **5**-Single drug regimen.

The tests of significance done were Spearman correlation, Chi-square and Independent sample Kruskal Wallis H test. For all the above tests, the level of significance was fixed at 5% (0.05) and p-values of less than 0.05 were considered statistically significant. Following the Kruskal Wallis test, a pair-wise comparison was performed in order to find out the differences in the outcome between different pairs of the above-mentioned five groups.

Bonferroni Corrected or adjusted p-values were calculated for each of the ten different pairs of categories. The p-value after Bonferroni adjustment is 0.049; which implied that the pair-wise comparisons with a p-value less than 0.049 will be considered statistically significant. The sample size calculated was 140, by using Medcalc online sample calculator, with type 1 error of 0.015 & a power of 90% with reference to the study "Incidence of Cisplatin induced Ototoxicity in adults in Head & Neck cancer" by Joshua B Greene et al, published in 2015.

Ethical Considerations:

Institute Ethics Committee clearance was obtained prior to the commencement of the study. A written informed consent was taken from all study participants and there was no financial burden on the study subjects.

Results

The study participants enrolled were 140, among which 91 were male & 49 were female. The mean age of the study population was 49.38 years with a SD of 14.45 years. The minimum age was 18 years & maximum age was 77 years. Around 60% of the study population were aged 51 years & above. The most common organ system involved among the study population was the gastrointestinal system. Only a quarter of the study population were found to have comorbidities. The other sociodemographic variables were not significant.

The analysis of hearing loss was done by PTA & DPOAE during the study. At baseline 77.1% of the study population had normal DPOAE & by the end of the study only 25.7 % of the study population had normal DPOAE (Fig.1).

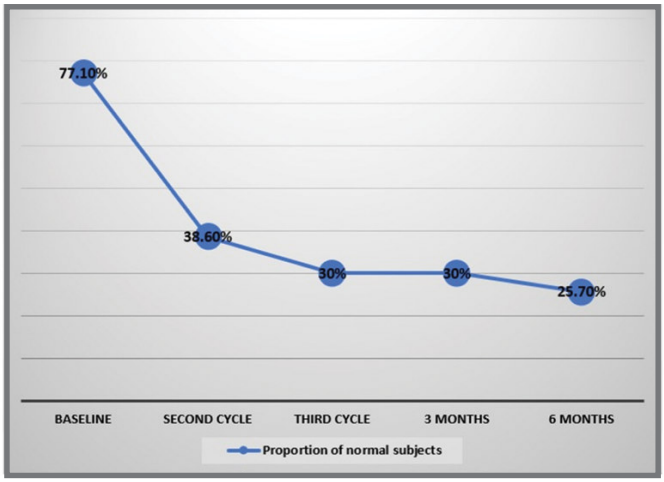

Fig. 1. Graph showing the normal proportion of the subjects after each cycle among the study population.

It was also observed that there was a gradual worsening pattern of hearing loss among the patients who received Taxanes, Platinum derivatives & patients who had received a combination of Platinum & Taxane derivatives (Fig. 2).

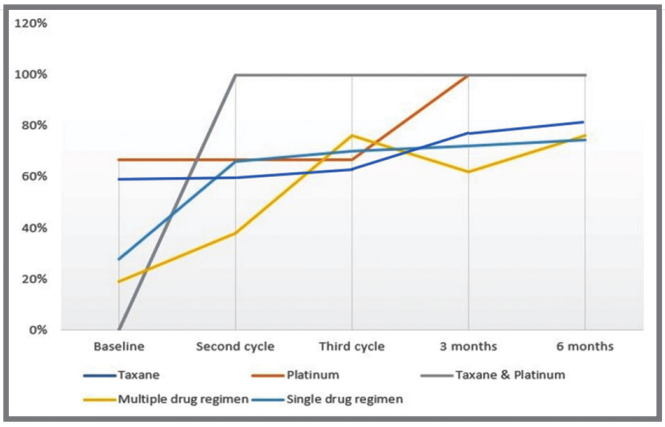

Fig. 2. Graph showing correlation of different antineoplastic drugs received & the hearing loss developed among the study population.

The analysis of hearing loss by PTA were done at baseline & speech frequencies, the overall median hearing loss at baseline & hearing loss with respective to

antineoplastic drugs received at high frequencies 4000Hz & 8000 Hz were calculated. The hearing loss calculated was graded with the NCI CTCAE ototoxicity grading scale for adults and children.

Among the study population who received platinum derivatives, the median hearing loss (Rt =20 dB, Lt=16.67dB) & had grade I ototoxicity. Taxanes & Platinum derivatives (Rt=16.67dB, Lt=10dB) & had grade I ototoxicity only on the right ear. The study subjects who had received carboplatin was found to have a median hearing loss (Rt = 18.33 dB, Lt = 15.83 dB) especially between audiometric assessment prior to the second & the third cycle. Also a median hearing loss (Rt =15.83, Lt = 15 dB) between the third cycle & the cycle at 03 months from the start of chemotherapy.

There was a significant hearing loss among the study subjects who received Platinum derivatives(15 to 35 dB), Taxanes(10 to 20 dB), Taxane & Platinum derivative combination (30 dB to 35dB) and for the patients who received multiple drug regimen(17.5dB).The hearing loss analysed were more pronounced at the higher frequencies at 4000Hz & 8000Hz.

The median hearing loss at 4000Hz among the study population who received Paclitaxel (Rt =15dB, Lt = 12.5dB),Cisplatin (Rt =15dB, Lt = 15dB) ,Platinum derivative & Taxane (Rt =10dB, Lt = 15dB) & Carboplatin (Rt =25dB, Lt = 27.5dB) was observed at the second cycle.

The median hearing loss at 8000Hz among the study population who received Paclitaxel (Rt =10dB, Lt = 15 dB), Platinum derivative & Taxane (Lt = 20 dB) & Carboplatin (Rt =25dB, Lt = 27.5dB) was observed at the third cycle. And the study subjects receiving Cisplatin had median hearing loss (Rt =20dB, Lt =20dB) at the end of 03 months. The median hearing loss assessed at higher frequencies 4000 Hz & 8000 Hz were statistically significant. Among the study population 19.3% reported tinnitus , 10% reported vertigo & 9.3% reported both tinnitus & vertigo.

Hearing at the baseline and hearing at the end of 6 months were tested for correlation using Spearmann correlation and was found to be positively correlated with a correlation co-efficient of 0.412 (p-value <0.01) in the right ear and 0.393 (p-value <0.01) in the left ear (Fig. 3 & 4)

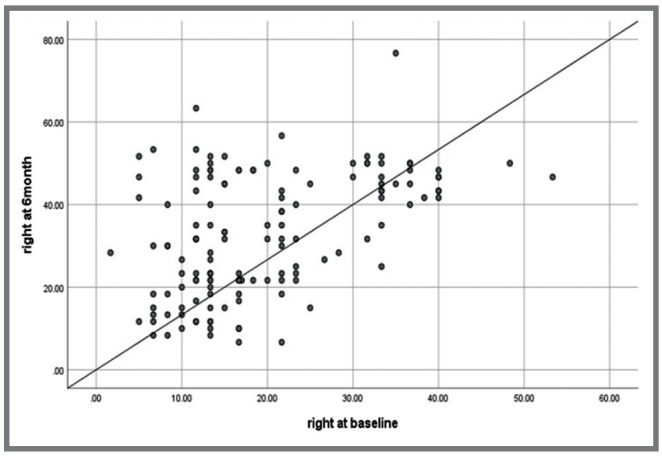

Fig. 3. Scatter plot to show correlation between hearing in the right ear at baseline and hearing at the end of 6 months.

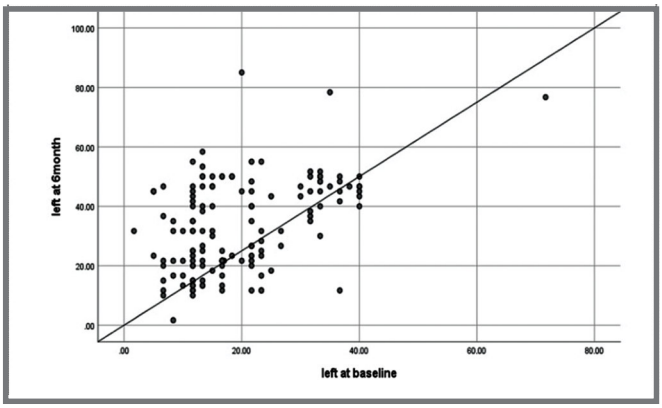

Fig. 4. Scatter plot to show correlation between hearing in the left ear at baseline and hearing at the end of 6 months.

Among the study population, Kruskal wallis H test & Bivariate analysis (Table I & Table II) were carried out & was found that the differences in median hearing loss between the groups of the pairs who received Platinum derivatives & single drug regimen , Taxane & Platinum derivative with any other single drug regimen, Any drug combination with any single drug regimen were statistically significant for the right ear (Fig. 5 & Fig. 6).

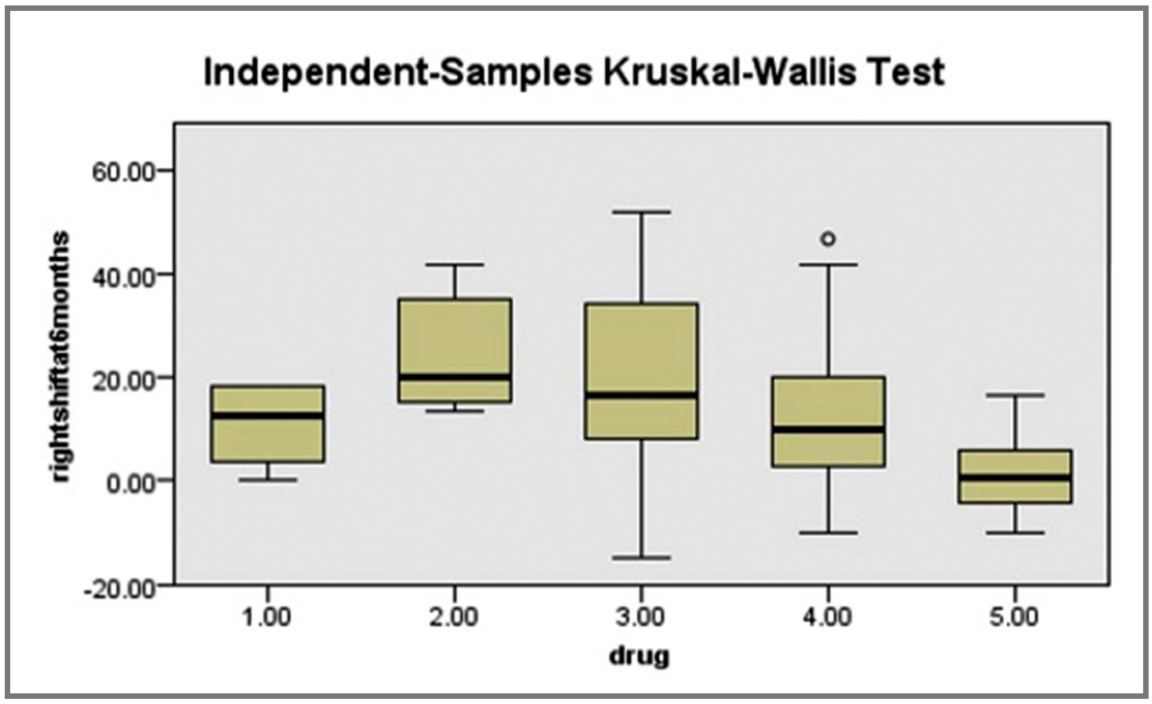

Fig. 5. Independent sample Kruskal-wallis Test on Right ear

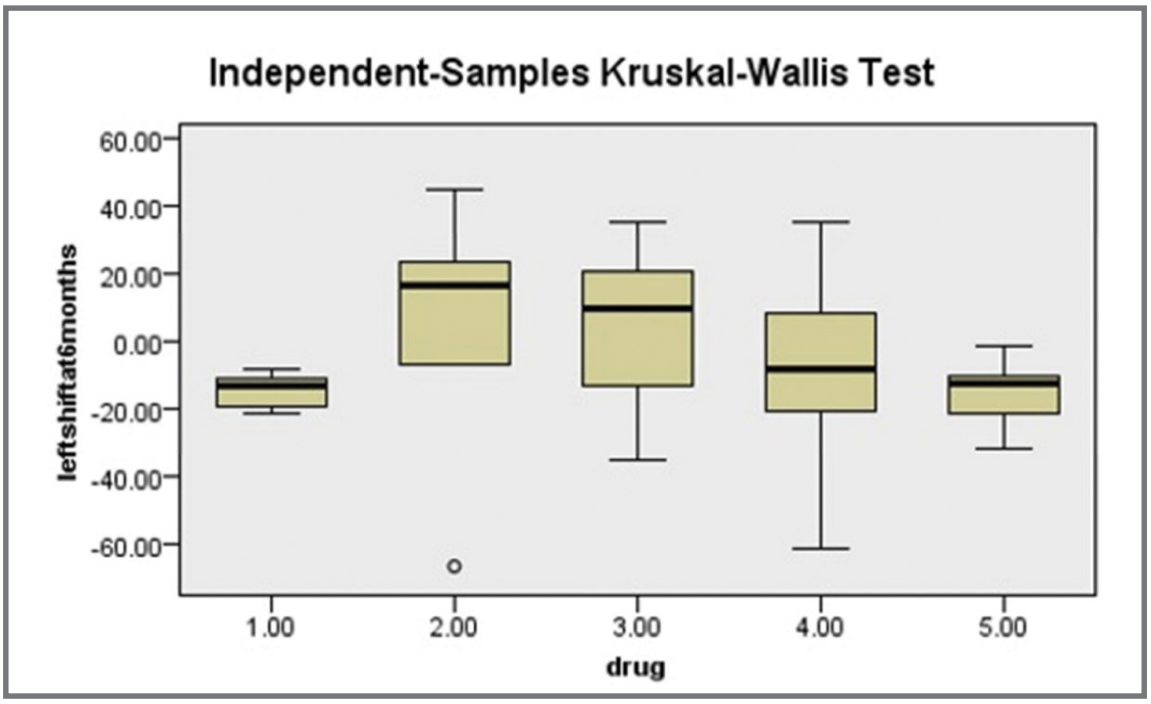

Fig. 6. Independent sample Kruskal-Wallis Test on Left ear

The median hearing loss relative to baseline between the groups in the left ear was not statistically significant although the median hearing loss when each group considered individually was found to be significant.

Table I: Results of an Independent Samples Kruskal Wallis H test in the Right ear – (Each row in the table tests the null hypothesis)

PAIRS (GROUP 1 - GROUP 2)	TEST STATISTIC	SIGNIFICANCE (P-VALUE)	
		OBTAINED	ADJUSTED
Group 1 and Group 5	36.917	0.068	0.684
Group 4 and Group 5	37.238	0.003	0.027
Group 3 and Group 5	57.77	0.000	0.001
Group 2 and Group 5	76.65	0.000	0.001
Group 1 and Group 4	-0.321	0.985	1.000
Group 1 and Group 3	-20.857	0.266	1.000
Group 1 and Group 2	-39.738	0.078	0.779
Group 3 and Group 4	20.536	0.036	0.357
Group 2 and Group 4	39.417	0.013	0.130
Group 2 and Group 3	18.881	0.286	1.000

Table II: Results of an Independent Samples Kruskal Wallis H test in the Left ear – (Each row in the table tests the null hypothesis)

PAIRS (GROUP 1 - GROUP 2)	TEST STATISTIC	SIGNIFICANCE (P-VALUE)	
		OBTAINED	ADJUSTED*
Group 1 and Group 5	0.042	0.998	1.000
Group 4 and Group 5	16.80	0.176	1.000
Group 3 and Group 5	39.79	0.007	0.067
Group 2 and Group 5	47.48	0.014	0.138
Group 1 and Group 4	-16.76	0.326	1.000
Group 1 and Group 3	-39.75	0.034	0.341
Group 1 and Group 2	-47.44	0.035	0.354
Group 3 and Group 4	22.99	0.019	0.188
Group 2 and Group 4	30.68	0.053	0.534
Group 2 and Group 3	7.69	0.664	1.000

* Bonferroni adjusted level of significance = 0.049.

Discussion

The chemotherapeutic agents commonly used and their mechanism of action is briefly discussed as below (Table : III)

At the assessment after 6 months, a total of 54 patients had significant hearing loss in the right ear and 25 had significant hearing loss in the left ear. The left ear was not affected alone, while 29 patients were affected in the right ear alone. Both the sides were affected in 29 patients, more frequently among the patients who received Platinum derivatives either singly or in combination with a Taxane.

The median hearing loss (140 patients tested = 280 ears tested) at frequencies 250 Hz, 500 Hz, 1000 Hz and 2000 Hz was 15dB, and at the end of 6 months at the same frequencies was 40 dB. At high frequencies 4000 Hz and 8000 Hz, the median hearing loss was 20 dB at the start of the cycle and at 6 months, it had worsened to 50 dB. This finding is comparable with the study done by Arora et al titled "Cisplatin based chemotherapy : Add high frequency audiometry in the regimen" where the threshold during the start of therapy was 54.4dB at all tested frequencies and 73.1dB after 3 months.[7]

Patients who had received Taxane alone had a median hearing loss of 12.5dB in the right ear. The median hearing loss was 20dB in the right ear and 16.67dB in the left ear for patients who received Platinum derivatives alone. For the patients who had received a combination of any Taxane and a Platinum derivative, was 16.67dB in the right ear and 10dB in the left ear. The hearing loss was found to be significant in patients who had received Platinum derivatives either singly or in combination.

At higher frequencies, patients receiving Taxanes or Platinum derivatives either singly or in combination were observed to have hearing loss too early when compared to the other drug groups. This finding is comparable with the finding in the study done by Arora et al, where the cohort which received Cisplatin, had moderate hearing loss relative to base line at higher frequencies.[7]

Table III: List of Chemotherapeutic drugs causing Otitoxicity – Adapted from Goodman & Gillman of Pharmacology -13 th edition

Other Antineoplastic Drugs	**EGFR inhibitor**	**Cetuximab**
	Platinum Derivatives	**Carboplatin, Cisplatin, Oxaliplatin.**
	Protein Kinase Inhibitors	**Dasatinib, Imatinib, Sorafenib, Sunitinib**
	HER 2 receptor inhibitor	**Trastuzumab**
Drugs Altering The Immune System Response	**Mefenamic Acid, Azathioprine, Tacrolimus**	
Immunomodulator	**Natalizumab**	
Sex Hormones	**Medroxy Progesterone Acetate, Norethisterone**	
Hormone Antagonist	**Letrozole, Toremifene**	
Prostate Cancer And Gonadotropin Releasing Antagonist	**Buserelin, Flutamide, Goserelin**	
Cytotoxic Drugs	**Vinca Alkaloids & Etoposide Vinblastine ,Vincristine, Vinde**	
Tyrosine Kinase Inhibitors	**Imatinib**	

Bivariable analysis was applied to find out association between age and gender with tinnitus & vertigo. But it did not yield statistically significant results implying that tinnitus and vertigo are independent of age or gender. Both tinnitus and vertigo showed an association with the category of drug received which was statistically significant (p-value <0.001).

Hearing at baseline was positively correlated with hearing at the end of the study & it was statistically significant. This is in contrast with the study done by Arora et al that there was no correlation between the baseline hearing level and cisplatin induced hearing loss. Hearing loss was significant numerically as well as statistically in both the ears between different categories of drugs. But the hearing loss was independent of age.

Among the patients who received Taxanes alone, 33.33% developed either tinnitus or vertigo or both following treatment In the study done by Sarfaraz et al, 3.88% patients developed either Tinnitus or Vertigo following Taxane therapy.[6]

The Kruskal wallis H test & Bivariate analysis for the study population were carried out & was found that the differences in median hearing loss between the groups of the following pairs were statistically significant only for the right ear & the left ear was not statistically significant. Although median hearing loss relative to baseline between the groups in the left ear was not statistically significant, the median hearing loss when each group considered separately was found to be significant. These results are in comparison with the study done by F.S Palatt et al which stated that "A recent publication where 200 study subjects were treated for childhood cancer with Cisplatin chemotherapy, caused hearing loss in 41.9% in the right ear & 47.3% in the left ears, with 11.6 times greater risk of hearing loss in the right ear and 17.6 times greater in the left ear, compared to the patients not treated with Cisplatin".[4] The limitation of the study is that the sample size for each drug category was not adequate enough to generalise all the findings obtained from the study, hence studies with greater number of participants are warranted.

Conclusion

Overall, this study adds to literature on the ototoxic adverse effects of chemotherapeutic agents. This study has however observed the ototoxicity with Taxanes alone or in combination with a Platinum derivative, which is in slight contrast to what is already known about Taxanes. Hence, high frequency audiometry along with DPOAE, could be established as a monitoring protocol for all patients receiving cancer chemotherapy.

Hence, it is recommended that patients on chemotherapy should be monitored for ototoxicity for early identification & early intervention or maybe even change in treatment protocols by replacing with less ototoxic drugs. It is recommended that there should be a clear ototoxicity monitoring protocol in all the centres where cancer chemotherapy is provided. This aids in identification of hearing loss at the earliest & could assist the patient & the patient's family to maintain effective communication, especially when the hearing deterioration had migrated into the speech frequencies. In those patients with severe hearing loss in young age the use of assistive learning devices could be recommended. The results of this study is consistent and generalised with other studies. There is no set ototoxicity monitoring protocol or ototoxicity grading scales till date. Hence further research is recommended in establishing a feasible ototoxicity monitoring protocol Nation-wide.

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Clinicopathological Spectrum of Benign Lesions of Larynx: A Prospective Observational Study

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Basavaraj Hiremath[1]

ABSTRACT

Introduction

Every human voice is unique because of anatomical, physiological, cultural, sociolinguistic and behavioural factors. Any disorder interfering with approximation, tension or vibration of vocal cord will change the quality, pitch and loudness of voice. The objective was to study the clinical profile, histopathological patterns and treatment options of benign lesions of the larynx.

Materials and Methods

A prospective observational study was conducted for 80 patients' clinically diagnosed as benign lesion of larynx. The inflammatory lesions were treated by conservative medical and speech therapy. Surgical intervention was done for neoplastic lesions of vocal cord.

Results

In our study, majority of patients 28 (35%) were between 21-30 years of age. Male preponderance was seen. Voice abuse in 53 cases was the common predisposing factor. The most frequent symptom Hoarseness or voice change together constituted 66 (82.5%), followed by vocal fatigue. Vocal cord polyp was the most frequent benign lesion in 17 (21.25%) patients, followed by vocal cord nodule in 14, chronic laryngitis in 8 and vocal cord palsy in 7 patients. Microlaryngeal surgery was done in 49 patients.

Conclusion

The vocal cord polyp is the commonest benign laryngeal lesions producing hoarseness in voice as the chief complaint. There was a high correlation between clinical and pathological diagnosis of benign lesions of larynx.

Keywords

Larynx; Benign Lesion; Hoarseness of Voice; Vocal Cord Polyp; Microlaryngeal Surgery

Larynx is an eloquent organ. The primary function of the larynx is to provide protection to the lower airway. It secondarily evolved to serve as a vocal generator of sound. The larynx lodges the vocal cords and ligaments which on vibration produces voice. Any disease or disorder which affects vibration will produce phonatory and laryngeal dysfunction.

Larynx can be involved with benign lesions of various causes such as infective, inflammatory, traumatic, neurogenic, congenital, functional and benign neoplasms.[1] A benign lesion of the larynx was defined by Hollinger as any mass of tissue in the larynx which does not present characteristics of malignancy.[2] The benign laryngeal lesions occur in a ratio of 2:3 to the malignant lesions. The common benign lesions of vocal cord are singer's nodule, polyps, papilloma, polypoidal degeneration and cysts. Others are sulcus vocalis, mucosal bridge, intracordal cysts and anterior webs. Some of these tumors may even undergo malignant changes like papilloma (4%), granular cell tumor (2%).[3,4]

Smoking, infection, voice abuse seems to be the most common causative factors of laryngeal lesions.[5] Inspite of the various etiologies, when diagnosed early and treated properly these lesions can have remarkable recovery. The

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aim of the present study was to study the clinical profile and histopathological patterns and treatment options of benign lesions of the larynx.

Materials and Methods

Study design: A prospective observational study was conducted for the patients came to the department of ENT and HNS with benign lesions of larynx. The study was done from Jan 2021 to March 2022. The sample size of the study was 80 cases.

Ethical clearance was obtained from Institutional ethical committee prior to the study. A written informed consent was obtained from the patients before their participation in the study.

Methodology: An observational study of 80 patients clinically diagnosed as cases of benign lesion of larynx was conducted in the department of Ear, Nose and Throat (ENT) at our tertiary care hospital. The malignant lesion of vocal cord and speech defect due to CNS lesions were excluded. Detailed routine ear, nose and throat examination of the patient with indirect laryngoscopy or video laryngoscopy was done. Diagnostic hematological, radiological and laryngoscopic investigations were done. This study describes the clinical profile and spectrum of diseases prevailing in this region. In the present study, the benign lesions are divided as inflammatory and neoplastic lesions, the inflammatory lesions were treated by conservative medical and speech therapy. Surgical intervention was done for neoplastic lesions of vocal cord.

Procedure: Microlaryngeal surgery (MLS)[6]: Patients were admitted a day before surgery after taking informed written consent. Surgery, to excise the lesion on vocal cord, was performed under general anaesthesia using a suspension video laryngoscope. The general surgical sequence was: general anaesthesia was given. The patient was placed in direct laryngoscopy position (Boyce position).The laryngoscope was placed and stabilised so that the glottis was clearly visualized. Under microscopic vision, the lesion was excised with cold steel conventional dissection i.e. truncation surgery was done. Haemostasis was achieved and laryngoscope was withdrawn after spraying the larynx with 10% xylocaine. There was no serious complication during and after microlaryngoscopic surgery. Excised lesion of vocal folds was preserved in 10% formalin and was sent for histopathological examination.

Post-operative Patients were advised strict voice rest for first 2 days post operatively. Oral antibiotics, anti-histaminics and proton pump inhibitors were prescribed. Patients were also advised steam inhalation and speech therapy for 3 months at the time of discharge and were kept on regular follow up. The preoperative and post operatively 4 weeks assessment of benign lesions of vocal folds for voice handicap was assessed by VHI-10 score. (Voice Handicap Index-VHI).[7]

Statistical Analysis: Data were pooled and analysed using SPSS v20 software. Data is compiled and described in tabular format.

Results

In the present study, majority of patients 28 (35%) were between 21-30 years of age, followed by 23 (28.75%) patients in 31-40 years of age. Youngest age of the patient was 8 years of age.

Males 44 (55%) were more commonly affected than females 36 (45%). Among the occupation, manual labourers (42.5%) were more affected by benign lesions of larynx followed by housewife (20%), teachers (17.5%) and students (17.5%).

Among the risk factors involved, voice abuse in 53 (66%) cases was found to be commonest habit as a predisposing factor, followed by smoking and alcohol in 26 (59%) cases in male population. Acid reflux was found in 18 (22%) cases.

Among the symptom distribution, hoarseness or voice change together constituted 66 (82.5%), was the most frequent symptom, followed by vocal fatigue in 14 (17%) patients. Reduced voice range was seen in 8 (10%) cases, foreign body sensation in 6 (7.5%) cases, aphonia in 3 (3.7%) and stridor in 1 (1.25%) of patients. Symptom distribution is shown in Table I.

In the present study, among the benign lesions of larynx, vocal cord polyp was the most frequently seen benign

lesion in 17 (21.25%) patients, next most common lesion was vocal cord nodule in 14 (17.5%) patients, followed by chronic laryngitis 8 (10%) and vocal cord palsy in 7 (8.75%) patients. Disease distribution is shown in Table II. The histopathological diagnosis of various lesions is described in Table III. Images showing histopathological sections of: a) vocal nodule, b) papilloma, c) laryngeal tuberculosis and d) Reinke's edema is shown in figure 1. All histopathological sections were stained with hematoxylin and eosin stain and observed under 20x magnification.

In the present study, management in the form of conservative treatment was done with medical therapy and speech therapy in 26 patients, anti-tubercular drugs in 2 patients. Among the surgical treatment, microlaryngeal surgery was done in 49 patients, 2 patients underwent open surgery and 1 patient needed stricture release procedure. Post treatment, complete recovery was seen in 71 (88.75%) patients, 7 (8.75%) patients had partial recovery of symptoms and recurrence of lesion was seen in 2 patients.

Post operatively VHI-10 score was recorded to determine improvement in voice of patients. Preoperatively mean VHI-10 was 23.60 ± 2.15 and it was 10.26 ± 1.42 postoperatively. Mean difference between preoperative and postoperative VHI-10 score was 10.84, depicting significant improvement in voice of the patients. The difference between pre and post-op VHI-10 was found to be statistically significant ($p < 0.01$)

Table I: Symptoms Distribution of Benign Lesions of larynx.

SL. NO	SYMPTOMS	NO. OF CASES (%)
1	Hoarseness or voice change	66 (82.5%)
2	Vocal fatigue	14 (17%)
3	Reduced voice range	8 (10%)
4	Foreign body sensation throat	6 (7.5%)
5	Aphonia	3 (3.7%)
6	Stridor	1 (1.25%)

Table II: Disease distribution of benign lesions of larynx

BENIGN LESIONS OF LARYNX	MALE	FEMALE	TOTAL	PERCENT %
Acute laryngitis	2	3	5	6.25
Adult papilloma	2	2	4	5
Chronic laryngitis	3	5	8	10
Habitual dysphonia	3	1	4	4
Haemangiopericytoma	0	1	1	1.25
Intubation granuloma	1	1	2	2.5
Keratosis	0	2	2	2.5
Laryngocele	0	1	1	1.25
Laryngeal stenosis	1	1	2	2.5
Recurrent respiratory papillomatosis	0	3	3	3.75
Reinke's edema	1	1	2	2.5
Sulcus vocalis	0	1	1	1.25
Tuberculosis larynx	1	3	4	5
Vocal cyst	1	2	3	3.75
Vocal cord nodule	9	5	14	17.5
Vocal cord palsy	2	5	7	8.75
Vocal cord polyp	10	7	17	21.25
Total	36	44	80	100

Table III: Histopathological Diagnosis of Benign Lesions

SL. NO	LESIONS	HISTOPATHOLOGICAL DIAGNOSIS
1	Vocal cord polyp	Chronic inflammatory tissue with hyperplasia and edema
2	Vocal cord nodule	Epithelial type hyperplasia
3	Chronic laryngitis	Epithelial hyperplasia with dilated vessels and mononuclear cell infiltration.
4	Adult papilloma	Fibrovascular core covered by squamous epithelium.
5	Vocal cyst	Columnar epithelium with mucus.
6	Reinke's edema	Edema of subepithelial space.
7	Keratosis	Thickened mucosa with reactive squamous epithelial hyperplasia.

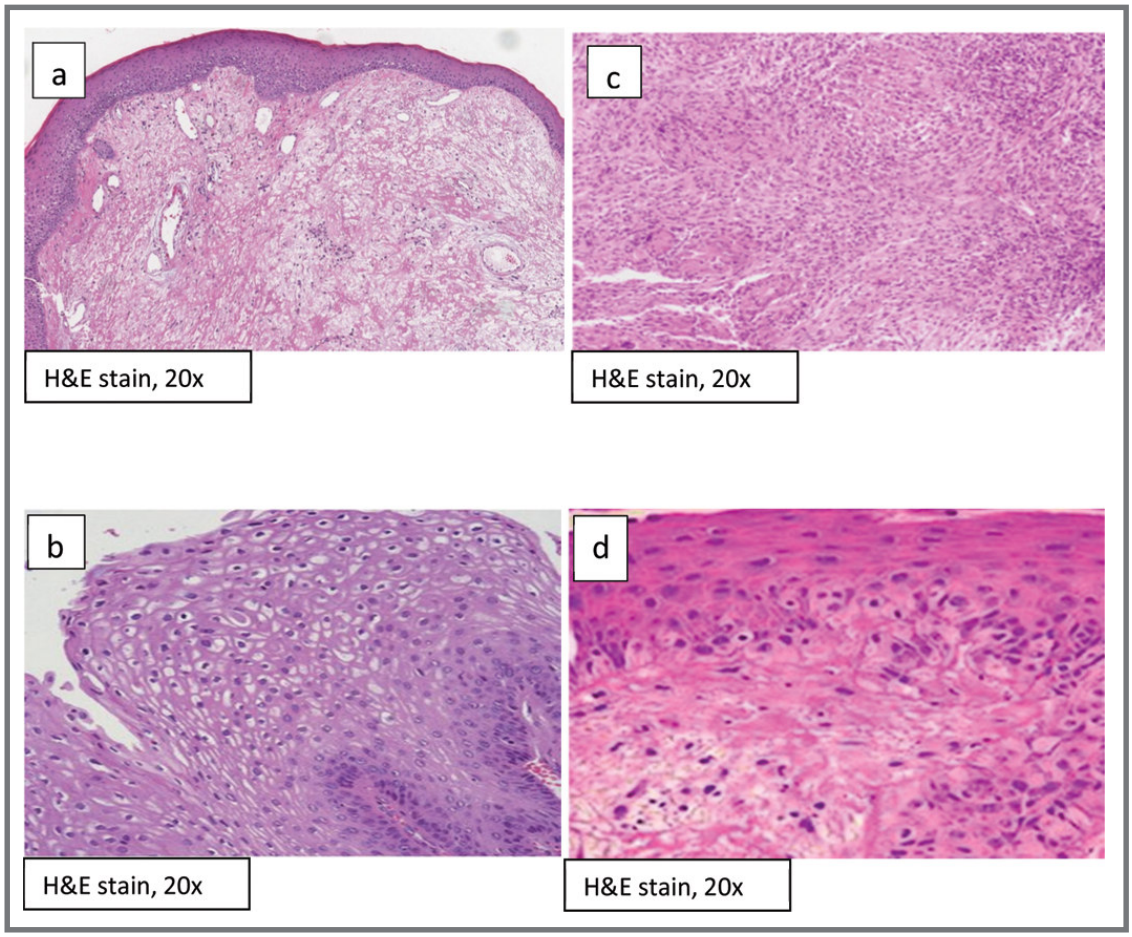

Fig. 1. Images showing histopathological sections of: a) vocal nodule, b) papilloma, c) laryngeal tuberculosis and d) Reinke's edema.

Discussion

In 1938, New and Erich published the Mayo Clinic experience of presenting with benign laryngeal lesions. They proposed that as true proliferative neoplasms were often clinically indistinguishable from nonproliferative inflammatory or hyperplastic growths, the term benign tumor should be used to encompass all abnormal growth of tissue in the larynx that lacked malignant or metastatic properties. Since then, some authors have revised the concept, classifying vocal fold nodules, polyps, cyst and nonspecific granulomas to be mucosal reactive inflammatory disorders and therefore nonneoplastic in nature.

In the present study, majority of patients 28 (35%) were between 21-30 years of age, followed by 23 (28.75%) patients in 31-40 years of age. Youngest age of the patient was 8 years of age. Our observation is supported by Hegde MC et al.[8] and Singhal P et al.,[9] who also reported maximum number of the patient in the age group of 20 to 40 years.

Benign lesions of larynx were found to be more common in males (i.e. 44 cases; 55%). These results were comparable with the other study by Wani et al[10] and Batra et al[11]. The male preponderance could be attributed to vocal overuse, occupation and smoking and drinking alcohol habits in the males. Prakash et al showed male to female ratio of 2.5:1.[12] Study by Shaha et al.[13] showed a female preponderance in cases of vocal cord nodules.

Among the occupation, manual labourers (42.5%) were more affected by benign lesions of larynx followed by housewife (20%), teachers (17.5%) and students (17.5%). Singhal P et al.[9] in their study, observed benign tumours of larynx among professional voice users and teachers (16%), salesman (16%) politicians (4%), bus conductors (6%) which were similar to our study. Chopra et al.[14] noted highest incident in housewives (25.3%), followed by shopkeepers (16.4%), businessmen (14.9%), students (12%), and teachers (10.4%), farmers (5.97%), salesman (3%) and others (10%).

Vocal abuse describes vocal behaviors associated with normal voice quality that often leads to vocal fold abnormalities and resultant dysphonia. In present study, vocal abuse was found to be commonest habit 53 (66%) present both in males and females as a predisposing factor followed by smoking and alcohol habits in 26 (59%) males. In a study by Ghosh et al.,[15] 72% patient had vocal abuse/ overuse as predisposing factor. Wani et al.[10] also quoted 56% cases with vocal abuse.

The other contributory factors were dyspepsia (22%), alcohol consumption and smoking (59%) and exposure to external irritants like smoke, dust, incense. Association of all risk factors with various lesions were studied, among which smoking and alcohol showed a strong relation in contributing to the lesions with a statistically significant p value. Prakash et al in their study supported the view that these lesions may also be caused by some sort of nonoccupational abuse of voice[12]. This group constituted 38% of the cases in their study. Tobacco smoke and alcohol acted as aggravating factors in the causation of most benign lesions.

Hoarseness is the commonest symptom and often the first symptom which brings the patient to the clinician. Among the symptom distribution, hoarseness or voice change together constituted 66 (82.5%), was the most frequent symptom, followed by vocal fatigue in 14 (17%) patients. Reduced voice range was seen in 8 (10%) cases, foreign body sensation in 6 (7.5%) cases, aphonia in 3 (3.7%) and stridor in 1 (1.25%) of patients. Mean duration of hoarseness with benign lesion of vocal cords observed were similar to various other studies. Cecatto et al.[16] found hoarseness was present in all cases (100%). Singh et al.[17] reported hoarseness in 69% cases

Lesions: Excessive mechanical trauma and stress in the midmembranous area of vocal cord leads on to wound formation occurs. Subsequently remodeling of the superficial layer of the lamina propria and to a lesser extent epithelium results in the formation of vocal cord nodules, polyps and cysts.

Vocal Cord Polyp : The most common lesion observed was vocal polyp (21.25%). Ten of them were pedunculated (62.5%) and seven (37.5%) were sessile. Two of them were of angiomatous type. All of the polyps were visualized videoendoscopically and MLS done. No recurrence was observed.

Vocal Cord Nodules : The second most common lesion observed was Vocal Nodule (17.5%). The lesion ranged from 1-4mm in size. Nine of them were less than 2 mm in size and five of them were less than 1mm in size. Eight were bilateral and six were unilateral lesion. Under video endoscopic control, all were excised. No recurrence was observed. McGlashen reported that vocal nodules were bilateral, small swellings (less than 3 mm in diameter) that develop on the free edge of the vocal cord at approximately the mid-membranous portion,[18] as was also observed in the present study.

Papilloma : Four cases of Papillomas were observed in this study (5%). The papillomas are solitary, small and less aggressive in behaviour. It occurs on the vocal cord, hence considered to be a true neoplasm of vocal cord. In two cases the mass was seen in the supra glottic region while in the other two, the lesions were seen occupying the vocal cords. In all cases under video endoscopic control, MLS was done. There was one case of recurrence, was observed after a follow up of 6-8 months.

Laryngitis due to gastro esophageal reflex disease is one of the established etiology, was mainly diagnosed with the associated symptoms and by ruling out other causes. They got symptomatic relief with medical therapy. In vocal cord palsy most common cause is idiopathic. Medical line of treatment was given and was followed up for 6 months for symptomatic improvement. Tuberculosis larynx more common in males. Most of them had congested mouse nibbling appearance of vocal cord. They were found to be sputum positive for Acid fast bacilli. Some of them had granulomatous lesion in the larynx which mimicked the growth. Tuberculosis lesion was confirmed by biopsy.

Hegde et al.[8] found vocal cord polyp in majority (40.47%), other lesion in decreasing order were vocal nodules (28.57%); tuberculosis of larynx (14.30%), laryngocele (4.76%), laryngeal web (4.76%), epiglottic cysts (4.76%) and subglottic hemangioma (2.38%). Singh et al.[17] reported most common lesion to be vocal polyp (40.7%), followed by nodule (28.4%), papilloma (22.2%) and cyst (0.05%).

In vocal Polyp, Kambic et al.[19] observed most common age group of 40–50 year, and female predominance (52%) as compared to males (48%). Martins et al.[20] reported vocal polyp more common in the age group of 41–60 years (51.31%) and reported slight preponderance among females.

On histopathological examination, we found a correlation of 92% between the clinical and pathological diagnoses. Nunes RB et al.[21] found 93.18% correlation whereas Wallis L et al.[22] found 91.5% correlation when compared their clinical diagnosis with histopathological diagnosis.

Management in our study was done with mainly by MLS. Surgery was the prime mode of treatment (61.25%) which is supported by Singhal et al (94%) and Hegde et al (83.29%). Post treatment, complete recovery was seen in 71(88.75%) patients, 7 (8.75%) patients had partial recovery of symptoms and recurrence of lesion was seen in 2 patients.

In our study, VHI-10 was used to assess the impact of voice complaints on patients' quality of life. It was easily self-administered and scored quickly at the time of evaluation. The difference between pre and post-op VHI-10 was found to be statistically significant ($p < 0.01$). Rosen et al.[23] noted statistically significant reductions in patients VHI scores following microsurgical excision and a program of pre and postoperative voice therapy.

Conclusion

A benign laryngeal lesion produces symptoms that can vary from mild hoarseness to life-threatening stridor. We conclude that the most common benign lesion causing hoarseness was the vocal cord polyps. The present study emphasises that it is not only the surgery that is important in managing vocal fold lesions but also certain life-style modifications like proper vocal hygiene, cessation of smoking, avoidance of alcohol play a vital role in reducing the incidence of these non-malignant laryngeal lesions significantly. Early diagnosis also leads to identification of malignancy in early stages and better prognosis. As such, the standard treatment of choice in all types of benign lesions of the larynx should consist of a triad of approach by micro laryngeal surgery (either microscopic or endoscopic, with or without the use of lasers and other

tools like coblator, microdebrider), voice rest and vocal rehabilitation.

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Main Article

A Study of Laryngopharyngeal Reflux Comparing Clinical Features with Endoscopy: Role of pH-Metry

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ABSTRACT

Introduction

Laryngopharyngeal reflux (LPR), now a known clinical entity is due to back flow of gastric contents into the upper aero-digestive tract (UADT). LPR is present in up to 50 % of patients with voice disorders.[1]

Materials and Methods

A total of 50 patients with symptom complex of voice disorders & chronic cough of unexplained origin were investigated at a tertiary care referral hospital with laryngeal endoscopy and 24 hours ambulatory double probe pH-metry to compare the clinical features before and after the treatment.

Results

A positive clinical endoscopic finding was seen in 74% whereas 80% showed positive acid reflux affecting the pharynx independently and/ or esophagus. Chronic cough of unknown origin (46 %) was the most predominant presenting symptom & posterior laryngeal erythema was the commonest endoscopic finding.

Conclusion

Chronic cough, persistent throat clearance and change of voice require to be investigated for LPR. Reflux Symptom Index (RSI) & Reflux Finding Score (RFS) are sensitive indices. 24 hour pH monitoring is a sensitive test for detecting LPR and is helpful to assess pre & post therapy outcomes. Positive pH probe studies help select patients who will respond to therapy and this avoids unnecessary treatment in other patients.

Keywords

Laryngopharyngeal Reflux (LPR); Double Probe pH-metry; Laryngeal Endoscopy

Laryngopharyngeal reflux (LPR), also known as supra-oesophageal reflux, extra-esophageal pharyngeal reflux disease & atypical reflux laryngitis, is now the most prevalent upper gastrointestinal (GI) & otolaryngological condition in clinical practice. A position statement of the Committee on Speech, Voice and Swallowing Disorders of the American Academy of Otolaryngology-Head and Neck Surgery outlines its symptoms, clinical manifestations, diagnosis & treatment and adopted the name "LPR" in 2002.[2]

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The symptoms of LPR include hoarseness, sore throat, throat irritation, difficult swallowing, chronic cough, globus pharyngeus, throat clearing, choking and difficulty in breathing.[3,4] In patients with gastro esophageal reflux disease (GERD) the main symptom is heart burn. Since the patients with LPR do not have the symptom of heart burn, gastric acidity is not considered either by the patient or their physician as the primary cause of their symptoms. LPR is related to but distinct from GERD.[5, 6, 7]

Gastric reflux occurs in 7% of the population on daily basis and 25% on monthly basis. GERD occurs in supine position & obese patients are at a higher risk of developing

it & have increased severity of symptoms.[8] LPR unlike GERD can also occur in non-obese patients & even in erect position. The reason for low incidence of heart burn in patients with LPR is that the laryngeal epithelium is more sensitive to gastric reflux than distal esophagus & therefore small amounts of reflux are capable of causing damage to the laryngeal mucosa while sparing esophageal mucosa & hence the symptom of heart burn may be absent. Touhil and Kulin have clearly mentioned the role of refluxed acid in the pathogenesis of laryngeal disorders.[9] The esophageal acid clearance mechanism also helps in the defense against the development of reflux esophagitis. Acid clearance normally occurs in two sequential steps. One or two peristaltic movements empty virtually all acid volume from the esophagus, leaving a minimal residual volume that sustains a low pH and then the residual acid is neutralized by swallowed saliva. The bicarbonate present in saliva has the ability to neutralize acid.[10] The symptoms of LPR can also occur via vagally mediated reflexes. However, esophageal dysmotility is an important cofactor in the extra-esophageal manifestations of GERD.[11]

The posterior glottis has the maximum impact of damage due to acid reflux. What leads to the initial inflammatory response is complex to imagine but the presence of pepsin in the reflux leads to worsening of the condition and the causation of symptoms & signs.[12, 13, 14] Another study by Galli et al suggested the role of bile reflux in the symptomatology & causation of LPR.[15]

The pathophysiology of GERD & LPR differs. The food from the oesophagus mixes with the acidic gastric juice in the stomach. Due to the relaxation of lower oesophageal sphincter (LES), some of this, gets intermittently leaked into the lower oesophagus. This episode termed as gastro esophageal reflux occasionally becomes pathological and constitutes GERD. The transient relaxation of LES up to 10-15 times a day for few seconds is normal, which increases the pH of lower oesophagus for short times and is physiological. However, whenever this gastric content crosses the Upper Esophageal Sphincter (UES) on to the unprotected laryngeal mucosa it causes damage & even a single episode of pH fall in the pharyngeal area is considered diagnostic of LPR. The detailed pathophysiology of LPR has been well described by Datta K et al.[16] Continuous pH monitoring studies are felt to be gold standards for study of LPR using probes that sense pH changes placed at different locations in the oesophagus & pharynx.[17] The general practitioners treat these patients empirically and symptomatically with antibiotics and supportive treatment for sore throat, allergic pharyngitis & pain throat, which may actually aggravate the condition due to use of antibiotics which cause gastritis. In these patients the only manifestations of reflux are upon the larynx. In GERD only LES is faulty while in LPR, UES is also malfunctioning.

Zerbib & Stoll have outlined diagnosis and treatment of LPR.[18] The diagnostic workup includes careful history, meticulous physical examination, nasopharyngo-laryngoscopy, upper GI endoscopy, radionucleide scanning and pH monitoring tests. Dual probes are used, with one probe 2.5 cm below the upper oesophageal sphincter & one 2.5 cm above the upper oesophageal sphincter to detect reflux in laryngopharynx. Awareness & importance of LPR can be gauged by the suggestion that up to 50% of all patients suffering from hoarseness and voice disorders may have significant LPR. The stress and strain of life, dietary irregularities and life styles may have made individuals more prone to this relatively new disorder and hence it was felt that a clinical study comparing clinical features with endoscopic studies & the role of ph metry before & after treatment would be noteworthy.

Materials and Methods

The study was carried out in a tertiary care referral hospital ENT centre for two years wherein a total of fifty patients with preset inclusion criteria were included in the study.

A. Inclusion criteria:

The patients with following symptoms of unknown cause i.e. persistent hoarseness of voice, chronic cough without URI or allergy, use of anti-hypertensives, feeling of obstruction in throat, laryngospasm /choking, chronic throat clearing,

difficulty in swallowing, post nasal drip without any nasal pathology/allergy, halitosis & frequent sore throat were included.

The Belafasky Reflux Symptom Index (RSI) (Table I)[19] based on a questionnaire listing various symptoms ranked from 0 (no problem) to 5 (severe problem) in the past month affecting the patient was considered to label the clinical scoring. **An index score of more than 10 was considered positive for LPRD**.

Table I: The Reflux Symptom Index (RSI)

FINDING						
Within the last Month, how did the following problems affect you?	**0 = no problem 5 = severe problem**					
1. Hoarseness or a problem with your voice	**0**	**1**	**2**	**3**	**4**	**5**
2. Clearing your throat	**0**	**1**	**2**	**3**	**4**	**5**
3. Excess throat mucus or post nasal drip	**0**	**1**	**2**	**3**	**4**	**5**
4. Difficulty swallowing food, liquid, or pills	**0**	**1**	**2**	**3**	**4**	**5**
5. Coughing after you ate or lying down	**0**	**1**	**2**	**3**	**4**	**5**
6. Breathing difficulties or choking episodes	**0**	**1**	**2**	**3**	**4**	**5**
7. Troublesome or annoying cough	**0**	**1**	**2**	**3**	**4**	**5**
8. Sensation of something sticking in your throat or a lump in your throat	**0**	**1**	**2**	**3**	**4**	**5**
9. Heartburn, chest pain, indigestion, or stomach acid coming up	**0**	**1**	**2**	**3**	**4**	**5**
Total						

Table-II : Belafasky Reflux Finding Score (RFS)

A	**Erythema**	**Arytenoids only - 2**	**Diffuse - 4**
B	**Ventricular edema**	**Partial - 2**	**Complete - 4**
C	**Subglottic edema**	**Absent - 0**	**Present - 2**
D	**Vocal fold edema**	**Mild - 1** **Moderate - 2**	**Severe - 3** **Polypoidal - 4**
E	**Diffuse laryngeal edema**	**Mild - 1** **Moderate - 2**	**Severe - 3** **Obstructing - 4**
F	**Posterior commissure hypertrophy**	**Mild - 1** **Moderate - 2**	**Severe - 3** **Obstructing - 4**
G	**Granuloma**	**Absent - 0**	**Present - 2**
H	**Thick endolaryngeal mucous**	**Absent - 0**	**Present - 2**

B. **Exclusion Criteria**

Children below 14 years, high risk cardiac patients, patient on medication known to alter esophageal motor function or gastric acid secretion, definite upper airway pathology, operated cases of duodenal, gastric & peptic ulcer and their perforations and GERD patients already on anti-reflux therapy & systemic diseases like hypothyroidism were excluded.

C. All patients were subjected to complete ENT exam including 90 degree rigid telescope examination / fiber-optic laryngoscopy & findings were recorded on proforma. Laryngeal findings were documented using Belfaskys Reflux Finding Score (RFS)[20] details as mentioned in Table - II.

D. All patients underwent dual channel ambulatory 24 hours continuous pH monitoring using Gastrograph Mk IV for pH-metry.

E. Patients were administered antireflux treatment for 16-24 weeks. Proton pump inhibitor (PPI) has been the main stay of treatment,[21, 22, 23] different studies using different PPIs. In our study, capsule Omeprazole 20 milligrams was given twice daily one hour before meals, supplemented with proper advice on dietary regulation including avoidance of excessive coffee & aerated drinks and other life style modifications i.e. time of meals, sleep timings and body weight reduction wherever required.[24] Some authors have used liquid alginate suspension in the treatment of LPR.[25, 26] However in our studies; we have not used liquid alginate suspension. Patients were evaluated at 2 weeks, 8 weeks, 16 weeks and 24 weeks intervals when clinical symptoms and signs were again documented. pH-metry was repeated at 24 weeks again.

Results

The followings observations have been made:-

1. **Age and Sex Distribution**: The ages of fifty patients was ranged from 14 yrs to 72 yrs. 56% were females (n=28) and 44% were males (n=22). Table III.
2. **Symptomatology & Diagnosis** is shown in Table-IV in order of occurrence.
3. **Laryngoscopic findings**: RFS was recorded in all patients, pretreatment and 24 weeks after treatment. The laryngoscopy findings are mentioned in Table V. The average RFS in patients with confirmed LPRD is shown in Table VI. A normal larynx & larynx with features of LPR are depicted in photographs for .The RFS reduced to <7 in 38 patients & 7-10 in 12 cases as compared to to RFS prior to treatment.
4. **Ambulatory 24 Hr pH metry:** Dual probe 24 hr pH monitoring was done in all the patients, some as inpatient & some as outpatient. Even one episode of pH value of less than 4 in proximal pharyngeal probe or pharyngeal and esophageal probes has been considered positive. The observed abnormal reflux in the various LPR diagnostic categories is shown in Table VII.
5. **Number of Reflux Episodes**: The number of reflux episodes of pH less than 4 in 24 hours period in positive cases of abnormal reflux of LPR is depicted as shown in Table VIII. The table IX shows the number of reflex episodes of less than 4 after 24 weeks of treatment.
6. Ten patients though clinically diagnosed, failed to elicit either of the two investigative positivity (endoscopic or pH metry) & were subjected to minimum of 2 weeks of anti reflux treatment. Three patients improved & were continued on treatment. Seven patients were advised to stop treatment and were dropped out of the study. Three patients (6%) who did not show any clinical findings endoscopically showed positive reflux by pH metry and improved symptomatically on anti reflux therapy. These were the patients who had 1- 3 episodes of reflux. This suggests that symptomatology has relationship with number of reflux episodes and appears much before endoscopic manifestations and those symptoms disappear much before endoscopic findings come back to normal as seen by Belafasky et al.[27]

Table III : Age and Sex Distribution

AGE IN YEARS	NUMBER OF FEMALES	NUMBER OF MALES	TOTAL
14-20	1	4	5 (10%)
21-30	5	4	9 (18%)
31-40	13	4	17 (34%)
41-50	6	4	10 (20%
51 and above	4	5	9 (18%)
Total	29 (58%)	21 (42%)	50

Table IV : Symptomatology & Diagnosis

S NO	DIAGNOSIS		NO OF CASES (%) N = 50
1.	Chronic Cough	CC	14 (28)
2.	Chronic throat clearing	CTC	12 (24)
3.	Hoarseness/change of voice	CV	9 (18)
4.	Globus Pharyngeus	GP	7 (14)
5.	Halitosis	H	4 (8)
6.	Frequent sore throat	FST	2 (4)
7.	Laryngospasm/choking	L	1 (2)
8.	Post Nasal drip	PND	1 (2)

Table V : Laryngoscpic Findings

FINDINGS		NUMBER OF PATIENTS (%) PRE TREATMENT N = 50	24 WEEKS
Erythema of Posterior Larynx	EPL	22(44%)	8/22 (36%)
Diffuse Laryngeal edema	DLE	3 (6%)	1/3 (33%)
Posterior Commissure Hypertrophy	PCH	5 (10%)	2/5 (40%)
Vocal fold edema	VFE	3 (6%)	0
Granulations	GR	3 (6%)	1/3 (33%)
Pseudo sulcus Vocalis	PSV	1 (2%)	0
		37 (74 %)	12/33 (36%)

After treatment the erythema of posterior larynx was the main feature on endoscopy.

Table VI : Average Reflux Findings score in confirmed LPR

TIME	SCORE			
	< 7	7-10	11-14	> 15
Pre-treatment	13	24	11	02
Post treatment (24 weeks)	38	12	-	-

Table VII : Diagnostic Categories by abnormal Reflux (Number of patients) abnormal Reflux

DIAGNOSIS	NORMAL	ESOPHAGEAL ONLY	PHARYNGEAL & OESOPHAGEAL	PHARYNGEAL ONLY	TOTAL
Hoarseness of voice	2	1	5	1	9
Chronic cough	2	0	9	3	14
Globus Pharyngeus	0	0	3	4	7
Chronic throat clearing	2	1	7	2	12
Post Nasal drip	0	0	1	0	1
Frequent sore throat	1	0	0	1	2
Halitosis	1	0	2	1	4
Laryngospasm	0	0	0	1	1
Total	8	2	27	13	50

Table VIII : No of Reflux episodes in LPR Episodes in LPR confirmed cases on PH Metry before treatment

NO OF EPISODES	NO OF PATIENTS
1 Episode	9
1-3 Episodes	11
3-5 Episodes	12
5 or more Episodes	8

Table IX : No of Reflux episodes in LPR confirmed cases on PH Metry after 24 weeks of treatment

NO OF EPISODES	NO OF PATIENTS
0 Episode	16
1 Episode	18
1-3 Episodes	4
3-5 Episodes	2
5 or more Episodes	0

Discussion

Gastro esophageal reflux into the laryngopharynx contributes significantly to a variety of upper respiratory problems. A good history and laryngeal endoscopy is critical to label the diagnosis of LPR & treat patients

The commonest symptom associated with LPR in our study was chronic cough of unexplained cause (28%). In a retrospective review of 216 patients who had positive probe studies, Fraser and Morton[28] found cough and hoarseness as the most common symptoms. Rival[29] and colleagues found that most frequent complaint was cervical dysphagia (35%) followed by globus (19%) and sore throat (17%).

The symptoms of 225 patients with GERD related conditions, hoarseness was found as 71%, chronic cough 51 %, globus pharyngeus 47 %, chronic throat clearance 42% and difficulty in swallowing 35% as seen by Koufman [30]. They demonstrated that Belafasky RSI score is reliable and valid. A RSI of 10 or more is associated with high likelihood of positive dual channel probe study. In our study only those patients, who on initial interrogation were found to have more than 10 score on RSI were included. Belafasky[20] in another study has proved that the RFS accurately documents treatment efficacy in patients with LPR. It demonstrates excellent inter and intra observer reproducibility. In their study, the RFS at entry was 11.5 (± 5.2 SD). This score improved to 9.3 (± 4.7 SD) at 2 months, 7.3 (± 5.5 SD) at 4 months, and 6.1 (± 5.2 SD) at 6 months of treatment. The mean RFS in our study group was 11.5 at entry which dropped to 6.1 after 06 months of treatment. This confirms with results of other authors like Beaver & Karow.[17]

In our study, 37 patients (74%) showed positive endoscopic findings of which erythema of the posterior larynx was the commonest occurring in 44% patients.

Postma[31] describes a review of patients with extra esophageal reflux (EER) who underwent dual probe pH testing, wherein 59% patients would have been inappropriately assumed to have a negative pH if their diagnosis was based solely on esophageal probe. In a similar study, Koufman[32] showed 11% patients had positive upper probe with normal esophageal pH probe findings. Little et al [33] showed importance of proximal probe in children and noted that 46% of subjects demonstrated positive EER by proximal probe in face of negative lower esophageal probe studies.

In our study, patients with RSI of more than 10 score, 40 (80%) patients had positive pH metry result; 13 patients (32.5%) had positive findings only in proximal probes with normal oesophageal probe and 27(67.5%) had both esophageal and pharyngeal positive result. In our series, 37 patients (74%) with RSI of more than 10 who were evaluated by pH monitoring were found to have LPR findings suggestive on endoscopy as well. In 30 patients the number of reflux episodes reduced following 24 weeks of treatment indicating a good response. Hanson et al[34] state a false negative rate of up to 50% because of small variation in probe placement. Other studies have documented that small percentage of normal subjects have proximal pH probes drops below 4. Contensin et al[35] have stated that pH drops below 4 may be too stringent in children. They have shown that pH drops of 6 are also significant in children. This is because pepsin which is critical in pathogenesis of tissue damage is active at pH levels up to 5.

Three patients who did not show any clinical findings endoscopically, showed positive reflux acidity by pH metry and improved symptomatically on anti reflux therapy. These were the patients who had 1- 3 episodes of reflux. One patient aged 14 presented with complaints of globus pharyngeus and frequent sore throat & this patient was confirmed to have LPR on pH monitoring. The patient was put on proton pump inhibitors and there was significant relief of symptoms.

Gastro esophageal reflux contributes to a variety of upper respiratory problems in children.[36] It has been suggested that GERD plays a major role in development of subglottic stenosis in paediatric age group, recurrent croup, apnoea, chronic cough, voice changes and hoarseness and probably sudden infant death syndrome. It is an important cofactor in laryngomalacia.

Conclusion

Chronic cough, persistent throat clearance and change of voice should be investigated for LPR to institute proper treatment. Reflux Symptom Index (RSI) & Reflux Finding Score (RFS) are reliable sensitive indices in our study. 24 Hour pH monitoring is a sensitive test in detecting LPR and is helpful to assess pre & post therapy response. Positive pH probe studies help select patients who will respond to therapy and avoid unnecessary treatment in other patients. A clinical protocol needs to be formulated and meticulously followed similarly in ENT centers for valuable record.[37] Symptomatology has relationship with number of reflux episodes. More the number of episodes of low pH, more severe are the symptoms. Symptoms of LPR may appear before endoscopic manifestations and get relieved much before endoscopic findings have disappeared after treatment. A stress on dietary regulations, reduction of body weight, regular exercise & avoidance of aerated drinks & coffee has helped the patients to avoid recurrence of symptoms. Twelve weeks of anti-reflux treatment is sufficient to improve the symptoms. However 24 weeks of treatment is required for symptoms to disappear completely. Occasionally patients with recurrence of symptoms require further medication.

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A Clinicomycological Analysis of Fungi Involved in Otomycosis

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ABSTRACT

Introduction

Otomycosis is a common infective condition of the external auditory canal caused by fungal species. It has a worldwide distribution yet its prevalence is greater in the tropical and subtropical region due to the climatic conditions.

Materials and Methods

Samples were collected from 200 patients who were suspected clinically of otomycosis and were subjected to mycological analysis. The study group included patients attending the ENT outpatient department in our institution.

Results

Of the 200 clinical samples that were evaluated, otomycosis was confirmed in 57% .The commonest symptoms were otalgia and aural pruritus. Injudicious use of antibiotic eardrops was the common predisposing factor followed by use of oil in the ear. Aspergillus niger was identified as the most common fungal species involved followed by Candida albicans.

Conclusion

Otomycosis is a very common diagnosis in the ORL (Otorhinolaryngology) outpatient department and highly refractory to treatment and associated with a variety of fungal agents. This clearly demonstrates that more studies related to otomycosis are necessary to provide effective treatment strategies directed at the individual agents.

Keywords

Otomycosis; Aspergillus; Fungi; Otalgia; Pruritus

Otomycosis refers to the superficial fungal infection of the external auditory canal.[1] Though it has a global distribution, the hot, humid and dusty environment of the tropical region makes it a more prevalent disease in these regions.[2,3] Otomycosis is mainly characterised by aural pruritus, otalgia, ear block, watery ear discharge[4] and is commonly seen in individuals with low socioeconomic status maintaining poor hygiene. The other predisposing factors include use of oil in the ear, injudicious use of ear drops,[5] history of prior ear infection and the habit of ear probing. Common etiological fungal agents include Aspergillus, Mucor and Candida while Aspergillus species are the most common causative agents.[6,7] The disease poses challenge to both the patient and the ENT (Ear Nose Throat) specialist since it requires long term treatment and follow up and moreover there could be recurrences.[8] Various factors related to the microorganism and the general and local characteristics of the patient are contributory factors of recurrence. The external auditory canal contains cerumen which is composed of lipids, proteins, free aminoacids, lysozyme and immunoglobulins which account for its antimycotic and bacteriostatic properties. The normal flora of external auditory canal includes a variety of bacteria as well as fungal species like Aspergillus and Candida. These floras of commensals are not pathogenic until the balance

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between fungi and bacteria are maintained. Alterations in the humidity, temperature, pH of EAC (external auditory canal), alteration in cerumen, systemic diseases, drug intake, environmental factors, previous history of ear infection or ear surgery all contribute to the disturbance of balance between bacteria and fungi.[9] Despite the fact that our climatic condition may favour otomycosis, literature search reveals that inadequate data exists on certain aspects of otomycosis like early resolution of symptoms, fungi specific treatment protocol and about preventing recurrences. In view of the high prevalence of otomycosis in our outpatient department, the study was planned to be carried out on the clinical features, predisposing factors and identification of fungal agents involved in otomycosis.

Materials and Methods

This was an observational study conducted in patients attending Otorhinolaryngology (ORL) Outpatient Department (OPD) in our institution. The study was carried out over a period of 12 months from January 2016 to December 2016. The study began after obtaining approval from the institutional ethical committee. Patients attending the OPD with ear complaints were examined using an otoscope. Clinically, diagnosis of otomycosis was established based on the presence of otomycotic debris in the EAC. Among these clinically suspected cases of otomycosis, 200 patients of age 18 years and above of either gender were selected by simple random sampling for the study. These patients were then enquired on history of watery ear discharge, ear block, aural pruritus, otalgia and hard of hearing. History of predisposing factors like swimming in ponds/lakes, injudicious use of antibiotic ear drops, use of oil in the ear and history of probing the ear canal using buds and pins was also obtained. Inclusion criteria included patients who satisfied the criteria for establishing a clinical diagnosis of otomycosis with otoscopic examination revealing grey white or curdy white discharge suspicious of otomycotic debris. Patients with history of trauma to the ear, ear surgery in the past, prior ear infection and immunocompromised state were included in the study. The samples were collected from the ear canal of these clinically suspected otomycosis patients using a sterile cotton swab. The samples were transported with the maintenance of the sterile condition to the microbiology lab for further mycological investigation. The fungal elements were identified by microscopic examination using 10% potassium hydroxide(KOH) preparation. Each sample was then inoculated on Sabaourad's Dextrose Agar media and growth on the media was confirmed by Lactophenol Cotton Blue Preparation. Outcomes measured were the clinical features, predisposing factors and identification of fungal agents involved in otomycosis. Statistical analysis was carried out in Microsoft excel and the prevalence of symptoms, prevalence of predisposing factors and the incidence of the fungal agents were expressed in percentage. Percentage estimation with 95% confidence intervals was carried out. Sample size in our study was taken in reference to the study done by Anwar K et al.[1]

Results

Of the 200 clinically suspected cases of otomycosis who were included in the study(number of patients) n =114 (57%) were microbiologically confirmed as otomycosis. Among these n = 69 (60.52%) were males and n = 45(39.47%) were females. Of the suspected otomycosis patients, n = 86 (43%) of the patients showed no growth in culture inspite of the symptomatology and presence of debris suspicious of otomycosis. The demographic characteristics are shown in Table I and gender distribution in patients who were positive for otomycosis is shown in Table II.

Table I : Demographic characteristics

AGE OF THE PATIENT (IN YEARS)	NUMBER (N=200)	PERCENTAGE OF TOTAL POPULATION
18-30	71	35.5%
30-50	97	48.5%
50 and above	32	16.0%
Gender		
Males	102	51.0%
Females	98	49.0%

Table II: Gender distribution in patients who were positive for otomycosis

POSITIVE FOR OTOMYCOSIS	NUMBER (N = 114)	PERCENTAGE
Males	69	60.52%
Females	45	39.47%

On analysing the clinical symptoms that these patients presented with, n = 111 (55.5%) of the patients had otalgia, n = 86 (43%) of the patients presented with aural pruritis and n = 80 (40%) of the patients with ear blocking sensation. n = 64 (32%) of the patients presented with ear discharge and n = 26 (13%) of the patients had hard of hearing which is shown in Table III.

Table III - Prevalence of symptoms

SYMPTOM	PREVALENCE IN %
Otalgia	n = 111 (55.5%)
Aural pruritis	n = 86 (43%)
Ear block	n = 80 (40%)
Ear discharge	n = 64 (32%)
Hard of hearing	n = 26 (13%)
Others (tinnitus)	n = 2 (1%)

*n stands for number of patients given in numerical number

Table IV : Prevalence of predisposing factors

PREDISPOSING FACTORS	PREVALENCE IN %
Use of antibiotic ear drops	n = 69 (34.5%)
Use of oil	n = 66 (33%)
Swimming	n = 35 (17.5%)
Prior ear infection	n = 22 (11%)
Diabetes	n = 19 (9.5%)
Trauma	n = 14 (7%)
Ear surgery	n = 8 (4%)
Immunocompromised state	n = 1 (0.5%)

*n stands for number of patients

The most common predisposing factors for an otomycotic infection of the ear canal in the study was identified to be the injudicious use of antibiotic ear drops contributing to n = 69 (34.5%) followed by the use of oil in the ear which contributes to n = 66 (33%). n = 35 (17.5%) had history of swimming, n = 22 (11%) had history of prior infection and n = 19 (9.5%) were diabetics. Those with prior history of ear trauma and ear surgery accounted to n = 14 (7%) and n = 8 (4%) respectively which is shown in Table IV.

Among the fungal species that were isolated n = 73 (36.5%) was Aspergillus niger (A. niger) and n = 59 (29.5%) was Candida albicans (C. albicans) and were the most commonly identified fungal species in our study. Candida non-albicans was cultured in n = 3 (1.5%). Of these n = 20 (10%) was Aspergillus flavus(A. flavus) and n = 3 (1.5%) was Yeast. Aspergillus niger coexisted with Candida in n = 2 (1%) and with Aspergillus flavus in n = 2 (1%). Aspergillus terreus was identified in n = 1 (0.5%) of the fungal cultures which is shown in Table V.

Table V - Incidence of fungal agents

FUNGAL SPECIES	INCIDENCE (%)
Aspergillus niger	n = 73 (36.5%)
Candida albicans	n = 59 (29.5%)
Aspergillus flavus	n = 20 (10%)
Candida non albicans	n = 3 (1.5%)
Yeast	n = 3 (1.5%)
Candida and Aspergillus niger	n = 2 (1%)
Aspergillus flavus and Aspergillus niger	n = 2 (1%)
Mucor	n = 2 (1%)
Aspergillus terreus	n = 1 (0.5%)
Clodosporium	n = 1 (0.5%)

*n stands for number of patients

Discussion

Otomycosis is superficial fungal infection of the external auditory canal. Though it has worldwide distribution, it is

more prevalent in the tropical and subtropical region because of the humid and warm climate. The disease is common during the rainy season compared to summer due to the moist conditions which favours the growth of fungus.[9-11] Majority of otomycosis presents as acute otitis externa but can persist to be a chronic presentation because of its refractoriness to treatment due to the involvement of various fungal agents. The fungi causing this infection are usually saprophytes and act as secondary invaders of tissue which become susceptible due to ear canal trauma, use of antibiotic ear drops, use of oil and other traditional medications. Other fungal infections in the body, poor nutritional status and hormonal changes can precipitate the infection or can cause flare-ups.[12,13]

200 cases of clinical otomycosis were included in our study, out of which 114 had positive fungal cultures contributing to n = 114 (57%). Paulose et al., had 171 positive isolates among 193 patients. Pradhan et al., had 87 positive samples out of 107 (79.45%).[14] Pahwa et al., cultured fungi in 47 samples out of 56 cases contributing to 83.9%.[15] Whereas Ahmed et al showed results similar to our study. Their study had 39 confirmed cases of otomycosis among 97 patients contributing to 40.2%.[16]

In our study, otalgia was the commonest symptom which was observed in n = 111 (55.5%) followed by aural pruritus in n = 86 (43%), ear block in n = 80 (40%) of patients and n = 64 (32%) had ear discharge. This matches the results of other studies. A study by Gokale et al., showed similar results with otalgia being the commonest symptom and aural pruritus as the second commonest.[16,17] A study by Pankti panchal et al., also showed otalgia and aural pruritus as commonest symptoms compared to other symptoms[18].

The most common predisposing factors in our study was the frequent and injudicious use of antibiotic ear drops followed by the use of oil in the ear contributing to n = 69 (34.5%) and n = 66 (33%) respectively. A similar study by Prasad et al., reported ear oil usage n = 63 (42%) as the commonest predisposing factor followed by history of self cleaning in n = 48 (32%) and use of ear drops in n = 30 (20%).[19]

In our study, fungal culture showed Aspergillus niger (A. niger) in 73 samples contributing to n = 73 (36.5%) followed by Candida albicans (C. albicans) species in 59 persons contributing to n = 59 (29.5%). Aspergillus terreus, Mucor and Clodosporium were detected each in n = 1 (0.5%), n = 2 (1%) and n = 1 (0.5%) respectively, Candida and A.niger in n=2(1%), A. flavus and A.niger in n = 2 (1%), Yeast and C. albicans in n = 3 (1.5%) respectively.

This matches the results of other studies by Martin et al., who also showed A. niger as the commonest followed by Aspergillus flavus (A. flavus) and Candida species.[20] Joy et al., carried out a study in 185 patients. A. niger was the most common fungal species in n = 82 (44.3%).[21]

In the study by Pahwa et al., 47 out of 56 samples tested positive for otomycosis and they isolated Aspergillus niger as the commonest in n =10 samples, Aspergillus fumigatus in n = 10 samples, A. flavus in n = 3 samples and Candida species in n = 2 samples. Paulose et al., reported 171 positive among 193 samples in which A. niger and A. fumigatus were the most commonly isolated fungi.

Similar to our study, a study by Kumar A et al., also showed A. niger as the commonest fungal species and was found in n = 53 (52.43%) samples. A. Fumigatus was cultured in n = 28 (34.14%), Candida albicans in n = 9 (11%), Candida pseudotropicalis in n = 1 (1.21%) and the remaining had Mucor species (n = 1).[22]

Co-infection with bacteria has also been reported and the commonly isolated bacterial species include Staphylococcus aureus, Coagulase negative staphylococci (CONS), Pseudomonas sp., Klebsiella and E.coli species. But bacterial isolation can be missed due to the use of antibiotic ear drops prior to taking the sample for culture. Kumar et al showed bacterial co-infection in 44 patients. The bacteria isolated were Coagulase negative staphylococci (CONS), Staphylococcus aureus, Pseudomonas sp., Escherichia coli and Klebsiella species. Some have reported the growth of other organisms as cause such as Acremonium sp., Fusarium sp., Penicillium sp., C. parasilosis, C. gulliermondi.[22]

Literature search reveals that there are variations between different studies in terms of presenting symptoms, predisposing factors, species identified, rate of recurrence and the response to treatment which has been reflected in our study values as well. These can be attributed to the effects of climatic and geographical conditions, social and economic differences which in turn influences the habits and hygiene of an individual within a society.[23]

Otomycosis is usually treated by suctioning out or syringing out the debris followed by the use of antifungal ear drops. These otomycosis patients can also present with a tympanic membrane perforation which becomes noticeable only after treating the disease and clearing the debris raises a question on the reaction of the tympanomeatal epithelium to the fungi.[24] Impaction of fungal debris in the most medial regions of EAC and avascular necrosis of tympanic membrane are attributed to as the reasons for tympanic membrane perforation in some cases. Both ears can be involved in immununo-compromised patients. External auditory canal osteitis has also been seen in these patients. Prior otological surgeries especially a mastoid cavity also acts as a risk factor for recurrent otomycosis. There is no specific treatment protocol and many medications are tried to treat this difficult to treat disease. Most fungal agents are responsive to clotrimazole[25-27] and fluconazole ear drops, yet the sensitivity varies depending of the type of fungi, the canal pH and previous treatment options employed. A similar study by Saraswathy et al., where antifungal susceptibility testing was done showed Candida isolates 100% sensitive to fluconazole and 95% to nystatin. Thus identifying the fungal agent by culture and establishing the antifungal susceptibility can help in promptly treating the disease thereby minimising hospital visits for treatment trials and in preventing recurrences.[28]

Limitations of the study are that bacterial isolates were not cultured from the obtained samples and bacterial co-infection was not studied. Though fungal species were identified, antifungal susceptibility testing was not carried out.

Conclusion

Otomycosis is a frequently witnessed condition in the outpatient department, still it remains challenging due to it's refractoriness to treatment and high incidence of recurrence and this is influenced by the hygiene status of the individual, work environment, the condition of the ear canal like the presence of cerumen, pH of ear canal and canal inflammation. Predisposing factors have to be enquired and proper awareness has to be given to the patient. Proper attention has to be given to all these factors while evaluating and treating a case of otomycosis. Fungi are ubiquitous in nature and the varied species involved in otomycosis necessitate the identification of the specific fungal agent so as to target the agent with highly sensitive antifungals in order to prevent the delay in complete resolution of symptoms and recurrence.

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Malignant Otitis Externa and Atypical Skull Base Osteomyelitis

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ABSTRACT

Introduction

Malignant otitis externa/ Skull base osteomyelitis is a common yet challenging disease to establish a diagnosis and manage efficiently to achieve a complete cure. We aimed to study the clinicopathological and radiological profile of Malignant Otitis Externa and atypical skull base osteomyelitis in the COVID-19 era.

Materials and Methods

Ours is a descriptive observational study conducted in an ambispective manner. It includes 11 patients diagnosed with either malignant otitis externa or atypical skull base osteomyelitis from 2015 to 2023. The clinicopathological, radiological, and management details of these patients were collected from their respective case sheets. The patients were followed up to learn their current status.

Results

Among the 11 patients, 4 were from the pre-COVID period, and the remaining 7 were from the post-COVID period. 10 patients had malignant otitis externa or lateral SBO, and 1 had atypical/Central skull base osteomyelitis. All the cases were associated with type II diabetes mellitus, with 64% relying on insulin. Otalgia (100%), otorrhea (82%), aural fullness (73%), vertigo (27%), and facial nerve palsy (18%) were the symptoms on presentation, and the external auditory canal granulation was seen in 82% on clinical examination. 82% of patients had an elevated erythrocyte sedimentation rate. Microbiology of the ear swabs revealed the growth of Pseudomonas aeruginosa in 36% of cases. 64% of patients had involvement mastoid seen in radiological imaging of the temporal bone. All the patients were treated as inpatients with long-term antibiotics and surgical debridement when needed, and the average duration of hospitalisation was 18 days.

Conclusion

Malignant otitis externa or skull base osteomyelitis can be diagnosed and managed adequately only when there is a high index of clinical suspicion in elderly diabetic patients with deep-seated earache. Meticulous clinical examination, serial documentation of clinical examination, ear swabs for culture and sensitivity, and imaging studies will help in staging the disease. The appropriate management includes histopathological examination of the EAC granulation tissue, followed by culture-sensitive antibiotics. Treatment must be monitored with regular Erythrocyte Sedimentation Rate levels and serial imaging of the temporal bone. Our study noted an apparent increase in Malignant otitis externa during the COVID-19 pandemic.

Keywords

Necrotizing Otitis Externa; Malignant Otitis Externa; Skull-Base Osteomyelitis; Diabetes Mellitus

Malignant otitis externa (MOE), synonymous with necrotizing otitis externa, invasive otitis externa or skull base osteomyelitis (SBO), is a common yet clinically challenging disease. MOE mainly affects the elderly diabetic population and the immunocompromised. It starts as an infection that initially involves the external auditory canal (EAC), which later spreads to the other regions of the temporal bone.[1]

Although there has been an attempt to understand the various clinical patterns of MOE, the literature is limited around the globe and also in India in regards to its incidence, risk factors, especially diabetes mellitus, clinical profile and lack of unified consensus on its management.

MOE was first reported by Toulmouche in 1838, after which Cohen and Friedman defined the diagnostic criteria and Carney provided a clinicopathological staging

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system.[1] The most common organisms causing MOE are Pseudomonas aeruginosa, Methicillin-resistant Staphylococcus aureus (MRSA), Klebsiella pneumoniae, Proteus mirabilis and also Aspergillus and Candida species.[2] The main line of treatment is culture-sensitive antibiotics for a prolonged period.[3] The role of surgery in this clinical entity is limited and is reserved for removal of sequestrum, drainage of abscess and the decompression of the facial nerve.[4]

MOE is classified as typical or classic lateral SBO and atypical or central SBO.[5] The atypical or central SBO is a relatively newer clinical entity that mainly involves the clivus or occipital bone and does not have the classical presentation of granulations in the EAC or temporal bone involvement, hence, the diagnosis may be delayed till radiological evaluation is done, as the tissue biopsy is often inaccessible.[6]

During the COVID-19 pandemic, there were quite a lot of changes in the treatment-seeking behaviour of patients, especially diabetics and their control of sugars. Our hospital, with limited infrastructure, had also noticed an increase in the number of cases of MOE and a case of atypical SBO in the post-pandemic period as noted by several other authors around the world.[7, 8]

We studied the clinicopathological and radiological profile of the MOE patients, the treatment protocols and their outcomes. We also tried to understand the factors that could have caused an apparent increase in the number of cases that were reported after the COVID-19 pandemic.

Materials and Methods

This is a single-centre ambispective observational descriptive study done in a tertiary care hospital from 2015 to 2023.

All the patients diagnosed and managed with MOE during this period were included. The details of 10 patients with MOE and 1 patient with atypical SBO were studied from their medical case records after obtaining appropriate permission from the hospital administration. The patients were followed up by contacting them over the telephone to know their current status.

The information regarding demographics, co-morbidities, signs and symptoms, COVID-19 vaccination history, examination findings done under otomicroscope (Fig.1), biochemical and microbiological tests, histopathology, imaging, management and follow-up were recorded.

Fig. 1. Granulation tissue seen along the floor of the External auditory canal with the surrounding area of congestion.

Biochemical parameters like ESR, renal and sugar profile were studied. Histopathological examination of the granulation tissue taken from the EAC demonstrated polymorphonuclear infiltration with inflammation with or without sequestrum (Fig. 2).

Given limited resources, nuclear imaging was not done, and all the patients underwent high-resolution computed tomography (HRCT) of the temporal bone and magnetic resonance imaging of the same (MRI) to understand the extent of the disease.

The severity of the disease was stratified as per Stevens et al protocol in which severe MOE exhibits either the presence of the facial nerve palsy or two or more clinical variables (other than facial nerve palsy) or two or more radiographic variables or 1 or more clinical variable

(other than facial nerve palsy) and 1 radiographic variable at the time of presentation.[9]

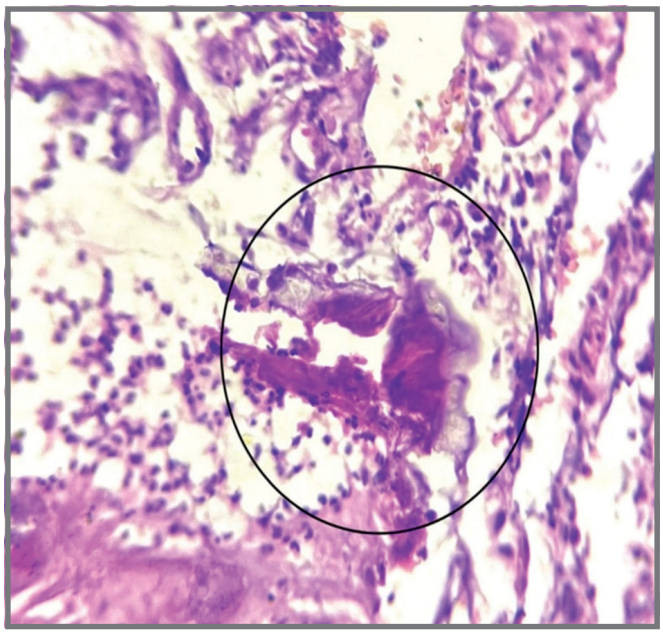

Fig. 2. Histopathological examination revealing sequestrum (within the circle) surrounded by dense infiltration of polymorphonuclear cells, lymphocytes and macrophages

The patients were treated with empirical third-generation cephalosporins for 6 weeks, which were later modified based on the culture sensitivity. The patients on follow-up were treated with oral fluoroquinolones, tablet Ciprofloxacin 750 mg twice daily for a period of 6 to 8 weeks. Supportive care included the management of otalgia according to the WHO step ladder pattern of pain management,[10] keeping the renal parameters of the patient as a concern and also good diabetic control that needed insulin administration in all 11 patients.

Furthermore, the impact of COVID-19 on the incidence, clinical profile and outcome of MOE patients was studied.

Results

Background and clinical characteristics (Table I)

Out of the 11 patients, 4 were from 2015 to 2019 (pre-COVID) and 7 from 2020 to 2023 (post-COVID) period. The sample had 8 male and 3 female patients, and their mean age at presentation was 58 years (range 40-72 years).

Clinical presentation

The right ear was more commonly affected (64%) than the left ear (36%), and none of our patients had bilateral involvement. 82% had deep-seated otalgia and purulent otorrhea, which were among the commonest symptoms, followed by aural fullness (73%), vertigo (27%), facial nerve palsy (18%) and other cranial nerve involvement (18%). Examination of the ear under otomicroscope revealed granulation tissue in the EAC in 82% of patients.

Comorbidities

All 11 patients had uncontrolled type II diabetes mellitus, with a mean duration of the disease being 14.18 years (range 3-30 years), for which 64% were dependent on insulin at the time of presentation. The mean blood sugar value was 251mg/dl at the time of admission and all 11 patients needed insulin during the hospital stay for adequate blood sugar control. The other co-morbidities seen in our patients were systemic hypertension (55%), chronic kidney disease (18%), dyslipidaemia (9%) and anaemia (9%). None of the patients were on immunosuppressants or had positive retroviral serology.

Laboratory tests

At the time of admission, a high ESR was seen among 82% pf patients with a mean of 54 mm/hr (range 10 - 110). 18.1% had a deranged renal profile and 9% had iron deficiency anaemia.

Microbiology

Ear swab was sent for culture and sensitivity from all 11 patients, and 36% had Pseudomonas aeruginosa, followed by Klebsiella pneumonia, Candida species and Methicillin-Resistant Staphylococcus Aureus (MRSA) seen in 9% each. 36% of the patients had no growth from the ear swab culture.

Table I: Clinico-pathological and radiological profile of MOE patients

Case No.	Age/Sex	Lat	Comorbidities	VX	Clinical findings	EAC finding	ESR (mm/hr)	HRCT/MRI	Organism	Antibiotics	DOH
1	46/M	R	DM, HTN, Dyslipidaemia	NA	Otalgia, otorrhoea	G	24	No significant involvement	P. aeuroginosa	CTX,AK	9
2	70/M	L	DM, Diabetic foot	NA	Otalgia, otorrhoea	–	26	No significant involvement	Candida albicans	CTX,MET	7
3	55/M	R	DM,HTN	NA	Otalgia, otorrhoea, hearing loss	G	100	No significant involvement	P. aeuroginosa	CTX,MET,CIP	14
4	71/M	R	DM,HTN	NA	Otalgia, otorrhoea, hearing loss, cranial nerve palsy (9,10,12)	G	110	Soft tissue density noted in the mastoid air cells	No growth	CTX,MET,CIP	22
5	59/M	L	DM,HTN	NA	Otalgia, hearing loss	G	55	Soft tissue density noted in the mastoid air cells	P. aeuroginosa	CTX,MET,PTZ	17
6	56/M	R	DM	Y	Otalgia, otorrhoea, hearing loss, Vertigo, Facial nerve palsy	G	10	Soft tissue density noted in the mastoid air cells with TMJ and ITF involvement	No growth	CTX,MET,PTZ	26
7	36/F	R	DM, IDA	Y	Otalgia, Vertigo, cranial nerve palsy (9,10,12)	–	40	No significant involvement	MRSA	CFT,LZ,GEN	6
8	65/F	L	DM,HTN	NA	Otalgia, otorrhoea, hearing loss	G	20	Soft tissue density noted in the mastoid air cells with TMJ and ITF involvement	No growth	CTX,CIP	25
9	55/F	L	DM,HTN, CKD	Y	Otalgia, otorrhoea, hearing loss, Vertigo	G	28	Soft tissue density noted in the mastoid air cells with ITF involvement	P. aeuroginosa	CTX,MET,CIP	23
10	58/M	R	DM	Y	Otalgia, otorrhoea, hearing loss, Vertigo, Facial nerve palsy	G	79	Soft tissue density noted in the mastoid air cells with TMJ and ITF involvement	K.pneumoniae	PTZ,MET	14
11	65/M	R	DM,CKD	Y	Otalgia, hearing loss	-	110	Soft tissue density seen in the retropharyngeal area with extension into the tegmen and nasopharynx	No growth	PTZ,MET,CIP	21

MOE : malignant otitis externa; M : Male; F : Female; Lat : Laterality; R : Right side; L : Left side; DM : Diabetes mellitus; HTN : Hypertension; CKD : Chronic kidney disease; VX : Vaccination for COVID-19; Y : Yes; NA : Not available; EAC : External auditory canal; G : Granulations; TMJ : Temporomandibular joint; ITF : Infratemporal fossa; ESR : Erythrocyte sedimentation rate; CTX : Cefotaxim; CFT : Ceftriaxone; PTZ : Piptaz; AK : Amikacin; MET : Metronidazole; LZ : Linezolid; CIP : Ciprofloxacin; GEN : Gentamycin; DOHS : Days of hospitalisation; $: Atypical skull base-osteomyelitis

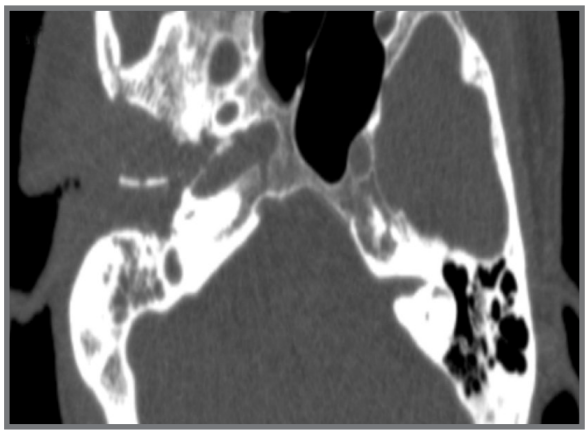

Fig. 3a. HRCT temporal bone showing erosion of the anterior canal wall extending into the TMJ, mastoid air cells

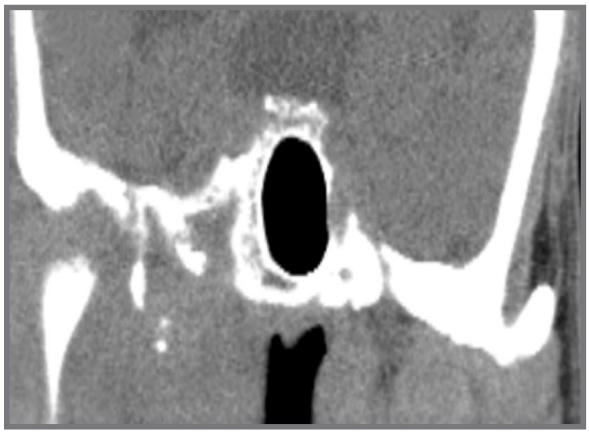

Fig. 3b. HRCT temporal bone showing erosion of the carotid canal.

Imaging

All the patients underwent HRCT of the temporal bone, and 64% of patients had soft tissue density and bony erosions involving the mastoid, followed by temporomandibular joint (TMJ) involvement in 36% and infratemporal fossa involvement in 27% (Fig. 3a & 3b). None of our patients had involvement of the petrous apex. HRCT imaging of the patient with atypical SBO showed fullness of the nasopharynx superior to the eustachian tube opening, along with irregularity of the bone in the inferior clival margin. The Contrast MRI of this patient revealed bone marrow changes involving the clivus (Fig. 4).

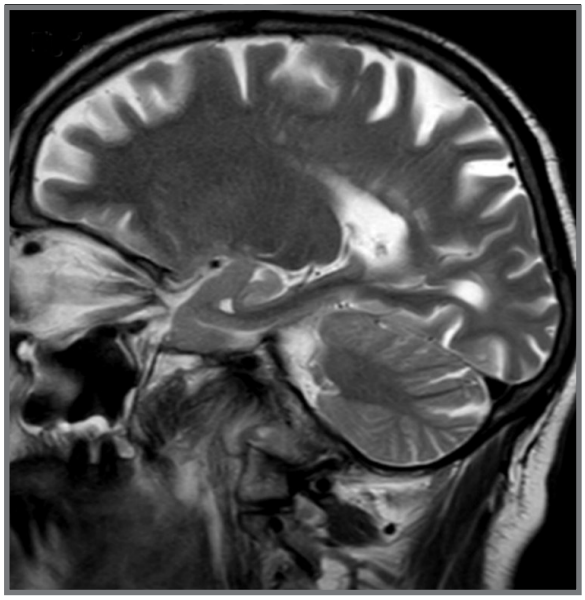

Fig. 4. Central or atypical skull base osteomyelitis MR image showing erosion noted in clivus and basi-occiput**.**

Treatment

All the patients were empirically started on intravenous cefotaxime followed by culture-specific antibiotics that included ciprofloxacin (45%), piperacillin-tazobactam (36%), amikacin (9%), linezolid (9%) and meropenem (9%). Topically they were given antibiotic ear drops like ciprofloxacin and gentamycin or dilute acetic acid ear drops as per the culture sensitivity pattern. The average duration of the treatment was 17.6 days.

Surgical management was reserved for cases that needed debulking of the granulation (40%) and facial nerve decompression (20%), done along with the drainage of micro-abscesses and the debridement of the diseased bone.

Outcome

All our study patients were clinically followed up for a period of 1 to 2 years of duration until they were symptom-free and clinically did not show granulations in the EAC. Of the total 11 patients, 5 had a severe MOE at the time

Table II : Severity and outcome of the disease

CASE NO	SEVERITY	DISEASE OUTCOME	FOLLOW-UP PERIOD
1	Non severe	Stable	Alive to date
2	Non severe	Stable	Alive to date
3	Non severe	Stable	Alive to date
4	Non severe	Expired	-
5	Non severe	Stable	Alive to date
6	Severe	Recalcitrant	Referred to the higher center
7	Non severe	Stable	Alive to date
8	Severe	Lost to follow up	-
9	Severe	Recalcitrant	Referred to the higher center
10	Severe	Stable	Alive to date
11	Severe	Expired	-

of admission (Table II). Post-treatment, 6 patients showed complete control of their MOE status and are alive to date, while 2 had a recalcitrant disease requiring referral to higher centres, 2 patients suffered mortality, and 1 patient was lost to follow-up.

Discussion

Chandler coined the term "Malignant" otitis externa because of its high mortality and morbidity during the pre-antibiotic era. The disease starts in the EAC and extends to the soft tissue and the periosteum, involving the skull base.[1]

The age of presentation, gender predilection and the laterality of the disease in our study were the 5th to 6th decade of life, with male preponderance and right-ear involvement, respectively which were similar to other studies.[11, 12] Uncontrolled type II diabetes mellitus followed by systemic hypertension were the commonly associated comorbid conditions, as in other studies done by Marina et al.[13, 14] Increasing age, along with uncontrolled sugars, is proposed to be a risk factor for MOE as it impairs phagocytosis and chemotaxis, leading to amplified virulence and the adherence of microorganisms to the cells. The lytic enzymes produced by the bacteria cause necrotizing endarteritis, which further leads to coagulation necrosis, granulation and microabscess formation, resulting in osteomyelitis, especially in patients with preexisting microangiopathy, as in cases with uncontrolled diabetes mellitus.[15, 16]

The clinical presentation of the patients in our study was similar to the studies around the globe, with deep-seated otalgia and purulent otorrhea being the most common symptoms, followed by aural fullness, facial nerve palsy and EAC granulations.[17, 18]

Although a non-specific inflammatory marker, ESR was elevated in 82% of patients and correlated well with the treatment response, as is also observed in studies by Rajasekar et al and Hasibi et al.[17, 18]

Pseudomonas aeruginosa was the most common organism seen in the ear swab culture study, and the other organisms found were Klebsiella pneumoniae, MRSA, Candida and Aspergillus species. However, there was no growth was noted in 36 %. These findings from ear swab culture were similar to the studies done by Loh et al and Vinayakumar et.al.[19, 20]

The mainstay of treatment for MOE is medical management with third-generation cephalosporins, fluoroquinolones, and carbapenems.[21] In our study, we tailored the use of antibiotics based on the antibiogram and in cases of no growth on the culture of the ear swab, an empirical treatment showed good results. Surgery was reserved for limited cases, similar to other studies such as biopsy of the granulation tissue in the EAC, removal of the sequestrum, drainage of the abscess, mastoidectomy and decompression of the facial nerve.[22, 23]

Although there is no unified protocol for the management of MOE, we recommend third-generation cephalosporins for a duration of 4 to 6 weeks and then follow up with oral fluoroquinolones like ciprofloxacin 750 mg twice daily for 8 to 10 weeks. This is also the recommendation as given by Lambor D et al.[25] We also recommend local therapy, such as topical ear drops that are culture-specific and dilute acetic acid ear wash. Surgical management is reserved only for biopsy, removal of sequestrum, to obtain core biopsy and microbiological samples, drainage of abscess or decompression of the facial nerve

While 55.5% had good treatment outcomes, around 36 % had relapsed and required readmission both for the disease and diabetic control, which was comparable to the study done by Glikson et al.[24] The mean duration of hospital stay was 18.2 days, akin to Lambor D et al.[25] We saw a mortality rate of 18% similar to Bhandary S et al,[26] although the mortality rate depends on various factors such as the patient factor, treatment factor and stage of the disease.

In our study, we observed certain patient factors that can be the cause for the poor outcomes such as older age, poor glycaemic control, multiple co-morbidities, multiple cranial nerve palsies and clivus involvement. These factors were similarly seen in the study by Lee et.al.[27]

The incidence rate of MOE was about 2.24 per million person-years of observation as per the study done by Yang et al and overall, the incidence of MOE is very less.[28] The COVID-19 era seems to have faced an apparent increase in the incidence of MOE as reported by Eweiss et al and many more are still being reported.[29,30] This can be because the pandemic had a great impact on patients with type II diabetes mellitus, and their glycaemic control, to the extent of causing immunosuppression as well. Although the clinicopathological and the radiological profile did not vary from the pre-covid MOE, the apparent increase in the number of cases should alert the surgeons, towards early clinical diagnosis, good control of sugars and appropriate treatment which is the cornerstone of management for this clinical entity.

Limitations

This is a single-center descriptive observational study with a small sample size, therefore, additional research in terms of a larger sample size and a multicentric study will help in a better understanding of the etiopathogenesis, disease activity, management protocols, treatment response and prognosis in MOE as well as in atypical SBO. However, while our sample size is small, the findings may reflect a national trend, and it may be an epiphany to this association between the post-COVID-19 pandemic and MOE.

Conclusion

Despite recent advances in diagnostic workup and treatment, MOE remains an obscure, highly unpredictable, serious and potentially fatal clinical condition. In our study, we observed poor outcomes in MOE patients of older age, poor glycaemic control, multiple co-morbidities, multiple cranial nerve palsies and clivus involvement. We advocate organism-specific antibiotics based on the ear swab culture. ESR and HRCT of the temporal bone, though non-specific, can guide us during treatment and follow-up. In our study, there was an apparent increase in the number of cases of MOE that were reported during the pandemic.

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Case Series

Management of Chondrosarcoma of the Mandible

https://doi.org/10.47210/bjohns.2024.v32i3.128

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ABSTRACT

Introduction

Head and neck chondrosarcomas are rare, typically affecting the anterior maxilla, sinonasal areas, and mandibular molar region. This study analyzes the clinicopathological characteristics of these tumors through three case presentations.

Case Series

This retrospective study included patients diagnosed with chondrosarcoma of the mandible who underwent tumor excision with subsequent reconstruction. All patients presented with rapidly progressing painless facial swelling, and biopsy revealed neoplasms arranged in lobules composed of spindle cells exhibiting moderate cytoplasm, pleomorphic vesicular nuclei, and prominent nucleoli demonstrating moderate nuclear atypia. Central chondroid matrix containing atypical chondrocytes in lacunae was observed, along with a mitotic rate of 7-8/10 hpf, areas of necrosis, calcification, and Ki-67 positivity.

Discussion

Early detection followed by radical surgical resection remains pivotal for achieving a favorable prognosis in mandibular chondrosarcoma. Given the high risk of recurrence, diligent long-term follow-up is imperative.

Keywords

Chondrosarcoma; Mandible; Head and Neck; Oral; Management

According to the World Health Organization (WHO), chondrosarcoma is classified as a malignant tumor characterized by pure hyaline cartilage differentiation, wherein tumor cells form cartilage without bone.[1] Head and neck chondrosarcoma is uncommon, comprising 5% to 12% of all chondrosarcoma cases. While virtually any craniofacial skeletal location can harbor this neoplasm, excluding the larynx, it predominantly manifests in the anterior maxilla and sinonasal structures.[2,3] The molar region of the mandible is reported as the most frequent site for mandibular chondrosarcoma.[4] However, the literature contains few published cases to date. At a tertiary care center, patients with chondrosarcoma of the mandible can benefit from access to advanced diagnostic and therapeutic modalities, as well as expertise from a multidisciplinary team experienced in managing complex head and neck malignancies. Through a coordinated and comprehensive approach, the aim is to achieve optimal oncological outcomes while preserving quality of life for the patient. This study seeks to analyze the clinicopathological characteristics of head and neck chondrosarcomas through the presentation of a series comprising three cases.

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Case Series

Three female patients, aged between 30 to 40 years, were diagnosed with chondrosarcoma of the mandible. They all presented with painless and rapidly progressive swelling over the face, persisting for 45 to 60 days. (Fig. 1)

Among them, two patients exhibited right-side disease while one patient had left-sided involvement. The tumors

Fig. 1. External Swelling

displayed an ulcero-infiltrative pattern, originating from the mandibular bone and extending to involve the entire half of the mandible along with the overlying skin. Additionally, all patients experienced loosening of teeth in the affected areas. (Figure 2)

Fig. 2. Intraoral Tumour

Fig. 3. Computed Tomography Scan

Contrast-enhanced computed tomography revealed erosion of the mandible. (Figure 3)

Nodal metastasis was absent in all cases. One patient underwent PET-CT, indicating an SUVmax of 25.3 for the primary lesion. Histopathological examination of biopsy specimens from two patients exhibited stratified squamous epithelium-lined skin, with deeper dermis revealing a lobulated neoplasm comprising a cartilaginous matrix with atypical chondrocytes in lacunae. Binucleated cells were observed, and spindle cells with nuclear atypia and myxoid stroma were noted at the periphery of the lobules. Mitotic activity ranged from 3-4/10 hpf. Immunohistochemistry showed Ki 67-10%, consistent with Grade I chondrosarcoma. The third patient exhibited similar findings, with higher mitotic activity (7-8/10 hpf) and areas of necrosis and calcification, indicative of grade III chondrosarcoma. Immunohistochemical staining was positive for CD99 and S-100. All patients underwent clinical assessment and were planned for surgical resection. Wide-local excision of lesions, including segmental mandibulectomy with involved skin, was performed in all cases. Reconstruction was undertaken using a free fibula osseo-cutaneous flap in one patient and a pectoralis major myocutaneous flap in the remaining

two patients. Final histopathological reports confirmed chondrosarcoma with free surgical margins. Adjuvant treatment was not administered to any patient. A minimum follow-up of 14 months revealed no signs of residual disease or recurrence.

Discussion

Chondrosarcoma, a malignancy characterized by a cartilage matrix, typically arises in facial bones, comprising 1–3% of all chondrosarcomas.[3] It tends to occur slightly more frequently in males, with a male-to-female ratio of 1.15:1. However, our case series notably featured exclusively female patients, with a mean age of 33 years (range: 2–82 years). The primary complaint, shared among our patients, was painless facial swelling, rapidly progressing over time.[3,4] While the literature commonly cites the maxilla as the most prevalent site for chondrosarcoma, our cases exclusively originated from the mandible.[5] Radiographically, chondrosarcomas often present as osteolytic lesions with radiolucent shadows and irregular borders. Advanced cases may exhibit a characteristic cloud-like matrix with calcified "whorls and arcs," accompanied by features such as endosteal scalloping, cortical disruption, periostitis, or soft tissue mass effect. Similarly, all cases in our series demonstrated gross mandibular destruction.[6] Chondrosarcomas typically manifest as large tumors exceeding 4 cm in size, characterized by a firm, mucoid, or gelatinous consistency with lobulated borders.[7,8] Evans' grading system stratifies chondrosarcomas based on cell density, nuclear size, staining, and mitosis. Grade I tumors display diverse lobular shapes with abundant hyaline cartilage matrix and low cellularity, while Grade II tumors exhibit increased cellularity and less chondroid matrix. Grade III tumors demonstrate high cellularity, marked nuclear atypia, pleomorphism, and extensive necrosis.[9] Differential diagnosis may include chondroblastic osteosarcoma, but the absence of osteoid and neoplastic bone helps differentiate chondrosarcoma. Notably, some chondrosarcomas may exhibit rapid growth following biopsy, emphasizing the need for prompt treatment post-biopsy. In light of a recent case within our patient cohort, where an individual experienced advancement of the condition following incision biopsy from the overlying skin at an external treatment facility, it underscores the importance of vigilance when encountering middle-aged patients presenting with rapidly progressing mandibular swelling, particularly in the absence of tobacco use. Such circumstances warrant a heightened suspicion for chondrosarcoma, given the potential implications of inadvertent involvement of surrounding tissues. Surgical resection with a wide margin (approximately 2-3 cm) remains the optimal treatment approach for mandibular chondrosarcomas. Chondrosarcoma typically displays radio and chemo resistance, rendering them ineffective. Neck dissection is generally unnecessary due to the tumor's low propensity for nodal metastasis.[10] However, a high-grade and recurrent tumor may lead to distant metastasis, commonly affecting the lungs, vertebrae, and sternum. Reconstructive options post-surgery may involve bone grafting with skin or soft tissue grafts. The five-year survival rates vary between grade I (approximately 90%) and combined grade II and III (around 50%) chondrosarcomas. Despite the relatively favorable prognosis, recurrence remains a concern, as observed in previous studies.[11] Fortunately, our patients did not develop recurrence or metastasis during the one-year follow-up period.

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Errata

Erratum
[Anatomical Attributes of Zuckerkandl Tubercle]

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Original Article

Anatomical Attributes of Zuckerkandl Tubercle
Geetha Rani B G, Soumya Vedavyasa, Shri Hari B G, Balachandra N
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Reason for Erratum

The affiliation for the second author, Soumya Vedavyasa, was stated incorrectly on page 67.

Incorrect affiliation
Department of Anatomy, Dr. B R Ambedkar Medical College and Hospital, Bangalore

Correct affiliation
Department of ENT, Dr. B R Ambedkar Medical College and Hospital, Bangalore

Explanation
The error was noted after publication. This error did not have any effect on the article.

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